HEART RATE AND RESPIRATION IN RELATION TO WORKING CAPACITY IN MAN

by

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CONTENTS

Part II. PHYSICAL WORKING CAPACITY IN MAN

INTRODUCTION

The heart rate, both during exercise and recovery has been much used for the assessment of working capacity (Johnson et al., 1942; Wahlund, 1948; and Åstrand, 1960), as an index of metabolic rate (Berggren and Christensen, 1950; Le Blanc, 1957; and Malhotra et al., 1963) and of fatigue (Brouha et al., 1963; and Maxfield and Brouha, 1963). Yet the heart rate has seldom been measured continuously throughout periods of exercise of differing intensity and recovery and then examined carefully in relation to working capacity in man. This is surprising, since all measures of work output and exercise tolerance which utilise the heart rate depend on it being either steady or changing at a predicted rate during the period of measurement.

During some experiments in which the heart rate was studied before, during and following exercise (in order to establish the reproducibility and reliability of this parameter in relation to the measurement of working capacity), it was noticed that in contrast to the uniformity of the heart rate during the steady state of exercise, large fluctuations in rate occurred at rest and more particularly during the recovery period. Occasionally, drops in heart rate of sixty to eighty beats per minute, together with rhythmical oscillations in rate were observed. The causes of these fluctuations, which were particularly striking during the recovery periods, seemed unidentifiable. They had, however, been recorded independently by Lamb (1963), and so it was felt that they were worthy of

further study.

In a preliminary investigation on forty-four subjects it was found that various patterns of heart rate were produced during recovery from a standard piece of exercise. These patterns were independent of age, sex and fitness. Different forms of exercise modified the response and, contrary to the findings of Lamb, it was suggested that the magnitude of the heart rate fluctuations was dependent on the subject's mode of respiration and thus might be an exaggerated form of sinus arrhythmia.

However, if this theory was correct, it was still a little difficult to explain why the large fluctuations in heart rate were present in some subjects and yet completely absent in others following the performance of an identical piece of exercise. It was thus felt necessary to conduct a further series of experiments to try and establish the precise relationship between the heart rate and respiration at rest and during the immediate post-exercise period.

For convenience, therefore, this thesis has been divided into two parts. The object of Part I is to examine further the respiratory variations in heart rate with special reference to the resting and exercise recovery periods before proceeding to Part II in which the heart rate as a measure of physical working capacity is considered.

Part I

RESPIRATORY VARIATIONS IN THE HEART RATE

CHAPTER 1

The resting heart rate

1.1. Physiological background

The original description of the relationship between heart rate and respiration was made by Ludwig in 1847, but it was not until the work of Anrep, Pascual and Rossler (1936) that the central and reflex causes of sinus arrhythmia were fully analysed. Before the publication of their study it was generally agreed that inspiration was accompanied by a rise, and expiration by a fall of the heart rate, but the mechanisms underlying respiratory cardiac arrhythmia were incompletely understood. Traube (1865) and Heymans (1929) attributed it solely to central influences; Herring, E. (1895) to reflexes arising within the lungs; whilst Bainbridge and Hilton (1918) and Bainbridge (1920) denied any direct effect of respiration on the heart rate and attributed the arrhythmia to reflexes arising indirectly as a result of blood pressure changes accompanying the respiratory movements.

The major contribution of Anrep and his co-workers was that they were able to examine the theories of these three schools and produce a comprehensive account of the central and reflex factors which govern the occurrence of sinus arrhythmia. Their experiments show conclusively that both central and reflex mechanisms were responsible for the observed respiratory rise and fall in the heart rate. In the first series of experiments performed on the dog "heart-lung-head" and innervated heart lung preparation they were able to demon-

strate, with the respiratory centre held in abeyance, that inspiration produced a rise in heart rate. The extent of the response was shown to depend on vagal tone and degree of inflation. The nerve endings of the pulmonary afferents were subject to adaptation which gave rise to a secondary slowing of the heart rate if inflation was maintained. In the second series they abolished all reflexes of pulmonary origin by sectioning the cervical vagi, respiratory activity being maintained by CO_2 tension in the blood perfusing the dog's head. If CO_2 tension was raised, the arrhythmia of the heart was shown to increase "pari passu" with the enhanced respiratory frequency. Thus, they were able to conclude that during inspiration the vagus centre came under two inhibitory influences which acted directly upon it, the one arising in the lungs and the other in the respiratory centre. In addition to this, the vagus centre was affected by the Hering-Breuer reflex indirectly..."thus each inflation affects the vagus centre in two opposite ways. On the one hand by a direct reflex it induces an inhibition of the vagus centre and on the other simultaneously but indirectly it antagonises this inhibition by cutting short the activity of the respiratory centre. Conversely, a deflation of the lungs diminishes the direct reflex inhibition of the vagus centre by cutting short the afferent impulses reaching it from the lungs, but at the same time it indirectly antagonises this effect by stimulating the activity of the respiratory centre."

The actual experiments of Anrep and his co-workers have never been repeated. Nevertheless, there is ample histological

(Berkley, 1893; Dogiel, 1903; and Larsell, 1921), electrophysiological (Adrian and Bronk, 1928; Paintal, 1952; and Widdicombe, 1952) and some indirect experimental (Lewis et al., 1943; Matthes and Ebeling, 1948; and Vanremoortere, 1949) evidence to support the existence of a stretch receptor mechanism responsible for the direct effect of lung inflation on the vagal centres, though it would seem, at least in the cat, that nearly all (90%) give rise to slowly adapting fibres (Paintal, 1952).

The contribution of central influences first demonstrated by Heymans (1929) and subsequently confirmed by Anrep have been recently reaffirmed by the interesting experiments of Joels and Samueloff (1956). Using anaesthetised animals in which the respiratory musculature had been paralysed with succinyl choline, they recorded the activity of the respiratory centre by sampling from the recurrent laryngeal nerve. During the cessation of respiratory movements the respiratory centre continued to discharge rhythmically and the heart rate showed accentuated arrhythmia in time with the discharge from the laryngeal nerve. They also reported phasic activity of the cervical sympathetic nerve in time with inspiratory activity of the motorneurones of the latter nerve. It is perhaps of interest that, although Anrep was not able to shed any light on this possible rôle of sympathetic accelerator fibres, Bronk (1934) two years prior to his study did show volleys from the inferior cardiac sympathetic nerve which were synchronous with inspiration.

Thus, despite the doubt surrounding the possible rôle of sympathetic afferent impulses, the description of sinus

arrhythmia as first described by Anrep and his co-workers still stands to-day and has found its way into most standard reference books, though it should be perhaps emphasised that their experiments were performed on heart-lung preparations in which reflex blood pressure changes had been purposely obliterated. These results, therefore, only strictly apply to experimental animals; to the author's knowledge no study has appeared in intact animals in which transient respiratory and circulatory events have been recorded and related directly to the phenomenon of sinus arrhythmia.

In man the technical difficulties of measuring instantaneous cardiovascular and neurophysiological changes are even greater than those in experimental animals. The picture of sinus arrhythmia, therefore, of necessity has had to be built up from a basis of empirical observation and its underlying mechanism inferred from indirect measurement. Nevertheless, until quite recently most authorities have agreed that the relationship between respiration and heart rate is similar in humans to that of the lower animals: Inspiration has been invariably associated with a rise in heart rate and expiration a fall, and a casual 1 : 1 relationship implied. For example, Scher (1960) "In the condition called sinus arrhythmia, common in children and young adults, the heart rate increases during inspiration and decreases during expiration." and Marshall (1961) ...."the heart rate increases towards the end of inspiration and slows towards the end of expiration. It is apparently due to alteration in vagal tone transferred from the central respiratory mechanism."

During the past few years, however, with the advent of more precise methods for monitoring heart rate and respiration, though some investigations have reported a 1 : 1 coupling between the two variables (Bucher and Baltig, 1956), an increasing number would appear to contradict this simple relationship. For instance, Matthes (1951) and Mechelke (1953) have found the opposite to be true with certain types of respiration: inspiration was often associated with a fall and expiration a rise in heart rate. Hustin (1953), too, showed that the relationship was not immutable and demonstrated the sensitivity of the cardiac rhythm to many respiratory factors, particularly those which affect the blood pressure, the pulmonary circulation and distribution of blood in the body. Bard (1961) noted from the unpublished data of Maxfield and Blythe that during normal respiration in one subject a reversal from increased to decreased pulse rate occurred during inspiration, but due to the fact that heart rate and respiration were not recorded continuously, no further detailed analysis was possible. These observations, nevertheless, find confirmation in the work of Manzotti (1958) who, in a series of carefully planned experiments, noted that a definite (5 sec.) lag existed between the respiration and the ensuing cardiac fluctuations. This result led him to suggest that the stretch receptor mechanism which has been shown to be responsible for sinus arrhythmia in animals was completely absent in man.

In an attempt to resolve these conflicting reports and the resultant confusion which has arisen, Clynes (1961) in

an extensive investigation re-examined the general basis of sinus arrhythmia in man, and using an analogue computer simulation technique he has put forward a completely new theory. He claims that during normal respiration two reflexes are involved; one sensitive to inspiration and one to expiration, both being biphasic and unidirectional, the form of the arrhythmia being the result of the superposition of these two transients and thus dependent on the depth and frequency of breathing. He further maintains that his results exclude the possibility of haemodynamic or central factors being responsible for the observed fluctuations, the changes being initiated by two separate stretch receptors situated in the lung cavity.

The theory of Clynes is of interest because it not only offers a physical explanation for some of the anomalies found by other workers at rest, but it also provides a possible quantitative basis for the large cardiac oscillation in the recovery heart rate previously noted (see p. 2). For, from a theory based on two separate reflexes one would expect different heart rate patterns to be produced, dependent on the subject's mode of respiration. At low respiratory rates well-defined fluctuations in heart rate should appear and even a 2 : 1 relationship observed, whereas at higher frequencies the two separate biphasic waveforms might not have time to complete themselves, leading to distortion and heart rate waves of small amplitude. In between these two extremes might not an optimum frequency occur during which the two reflexes summate to produce heart rate oscillations

of increased magnitude?

It was in order, therefore, to gain further information of the relationship between heart rate and respiration in general and to establish the accuracy and validity of the Clynes model of respiratory sinus arrhythmia in particular that the present investigation was carried out. Particular attention has been paid to the separate effects of inspiration and expiration on the heart rate and some attempt has been made to assess the possible contribution of haemodynamic factors to the underlying mechanism responsible for reflex control of sinus arrhythmia in man. The implications of the results are discussed in relation to the immediate post exercise period in Chapter 2.

TABLE I.

Physical characteristics of the ten experimental subjects.

Subject	Age (years)	Weight (kg.)	Height (cm.)
E.J.W.	24	80.0	175.3
M.G.R.	27	78.8	182.6
C.J.F.	22	72.1	184.2
A.V.P.M.	21	71.6	183.5
T.E.W.T.	23	68.8	179.1
D.R.H.	20	78.1	179.1
I.G.McC.	20	70.0	177.8
A.M.P.B.	24	64.0	168.3
I.S.B.	24	76.4	177.2
K.B.S.	31	73.5	170.2

1.2. Procedure

The heart rate and respiratory volume were measured continuously on ten subjects whose age, sex, weight and height are given in table I. These subjects reported to the laboratory at various times during the day and were asked to rest quietly in a chair for fifteen - twenty minutes before the electrodes and pneumotachograph screen were attached. Following this preliminary rest period, the various "step" (fast) and expiratory and respiratory "impulse" and "pulse" manoeuvres to be performed were explained to the subjects. Before each manoeuvre was carried out experimentally, time was set aside for practice, but during the actual experimental period the timing of all required events was given by the experimenter.

In order to perform the step inspiratory and expiratory manoeuvres correctly the subject was required to breathe in (or out) as quickly as possible and to hold that breath for a further fifteen seconds with the glottis open. Unfortunately, it soon became evident during preliminary experimental runs that this manoeuvre was more difficult to perform naturally than had at first been appreciated. However well the manoeuvre was explained and the importance of an open glottis stressed, it was found that the instructions were rarely carried out satisfactorily. Indirect measurement of the intrapulmonary pressure changes in the chest cavity using the oesophageal balloon technique of Mead and Whittenburger (1953) revealed that the glottis was invariably

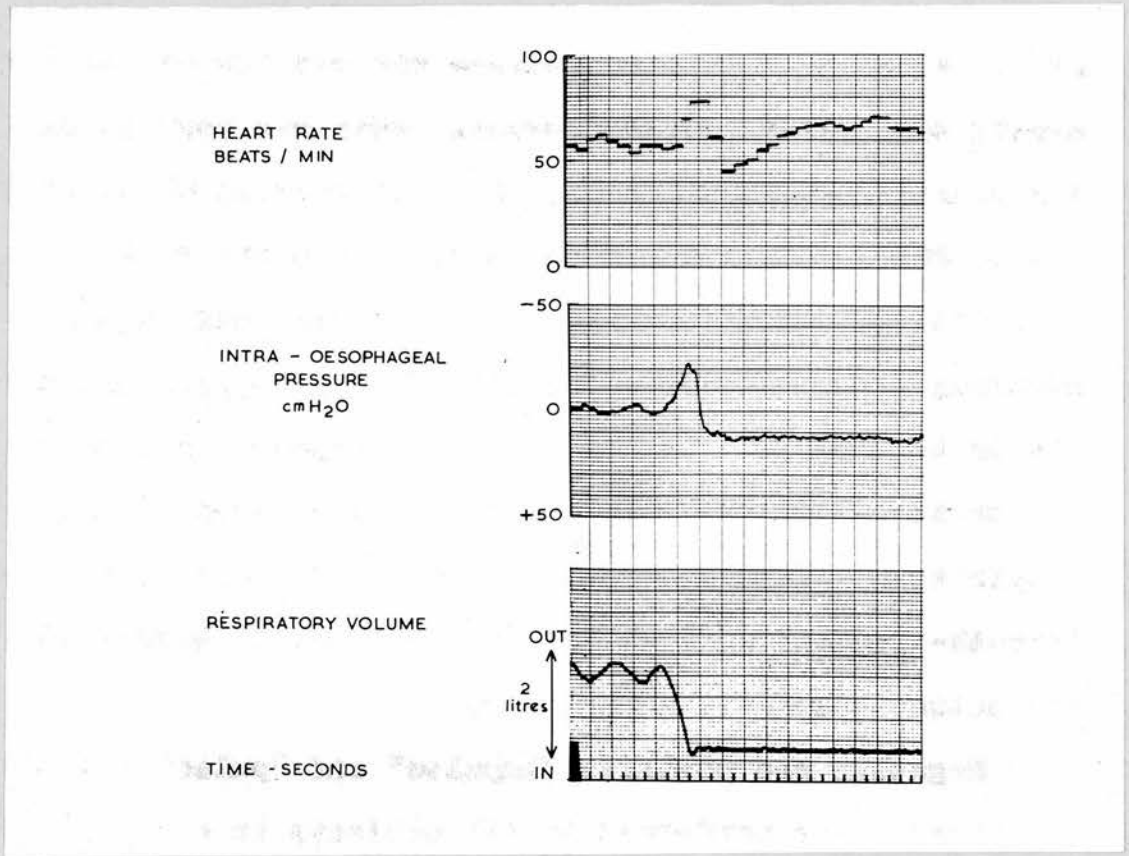


fig. 1. The relationship between heart rate, intra-oesophageal pressure and respiratory volume during a held inspiration. It will be noted that during the apnoeic period the intra-oesophageal pressure does not return to normal, but becomes decidedly positive due to subject closing his glottis.

(and often subconsciously) closed during the middle and latter part of the manoeuvre. This gave rise to unwanted pressure effects which masked the true response of the heart rate (fig. 1 cf. fig. 10).

To overcome this difficulty it was found necessary to devise a method that would ensure the glottis stayed open during the breath-holding period. This was done by allowing the subject to take a series of small breaths which allowed a very small volume of air to pass in and out of the lungs. This manoeuvre was found simple to perform and as well as ensuring that the glottis remained open, it maintained the air in the lungs at approximately atmospheric pressure during the breath-holding phase. To avoid interference from previous respiratory cycles the subject was asked to perform this "breath-holding" procedure for a few seconds before commencing the actual step respiratory effort.

Negative and positive "impulse" and "pulse" respiratory manoeuvres were performed by all subjects in a way similar to that described above. In the former, they were asked to breathe "out-in" or "in-out" as quickly as possible and to hold the breath and in the latter case to intersperse "in" and "out" phases with a period of breath-holding of various lengths in the form of a respiratory square wave.

In five subjects certain static positive and negative intrapulmonary pressure manoeuvres were also performed. These were measured using a Statham gauge. The pneumotachograph screen was held in the mouth and positive or negative pressure breath-holding was produced by the subject

placing his hand over the end of the screen and then blowing or sucking to the required pressure. By this means respiratory movements and pressures could be recorded simultaneously. A meter (that had been previously calibrated using a water manometer) was connected to the Statham gauge so that the subject could produce the given pressure whilst observing the meter throughout each manoeuvre.

The majority of the experiments were performed with the subjects sitting, but in two subjects additional manoeuvres were carried out in the supine position and also whilst standing.

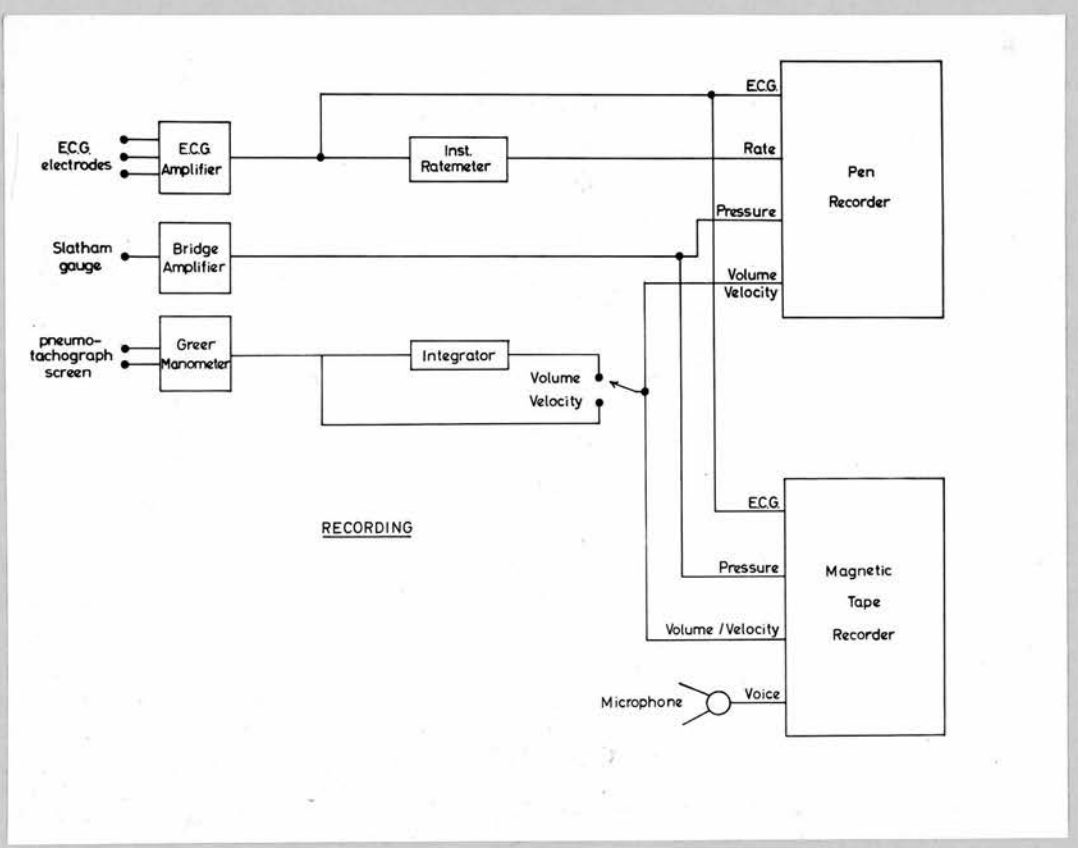


fig. 2. Block diagram of the recording procedure. All heart rate and respiratory data throughout the experiment was recorded simultaneously on magnetic tape and 4-channel recording paper.

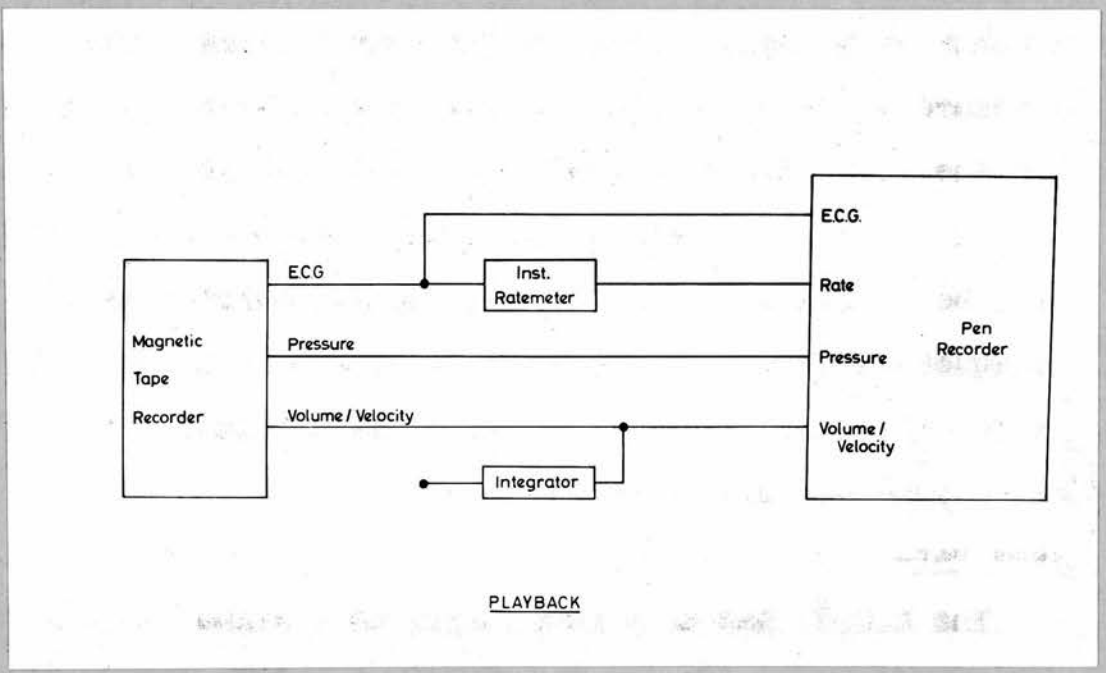


fig. 3. Block diagram of the procedure used for the playing back of the experimental records for subsequent analysis (see page 13).

1.3. Methods

The general arrangement of the instrumentation system is shown in figs. 2 and 3. A Devices 4-channel recorder was used to monitor the parameters under observation during the actual experimental period, the data being simultaneously recorded on three F.M. tracks of a magnetic tape recorder together with spoken notes on the fourth track. This method of recording data not only allowed the experimenter to play back the tapes and "re-live" the experiment at any time, but it allowed second thoughts concerning the way that any data might be handled. This was particularly helpful during the subsequent analysis of records. This linearity of the F.M. system was better than $\pm$ 1% full scale deflection overall, with a peak-to-peak noise level of 1%.

Heart rate

The E.C.G. has many advantages as a signal source for manual computation at rest, but during exercise a major problem is encountered: Unwanted noise produced both by body muscle and by electrode movement. The combined effect of these two factors on the exercise E.C.G. is shown in fig. 4. In order to make the record suitable for automatic analysis the high frequency E.M.G. potentials can be reduced by using an E.C.G. amplifier with a restricted band width, and by careful positioning of the electrodes on the body. For convenience in this study, the differential amplifier of Austin and Harris (1957) was rebuilt and the actual positioning of the electrodes used is as follows: Two

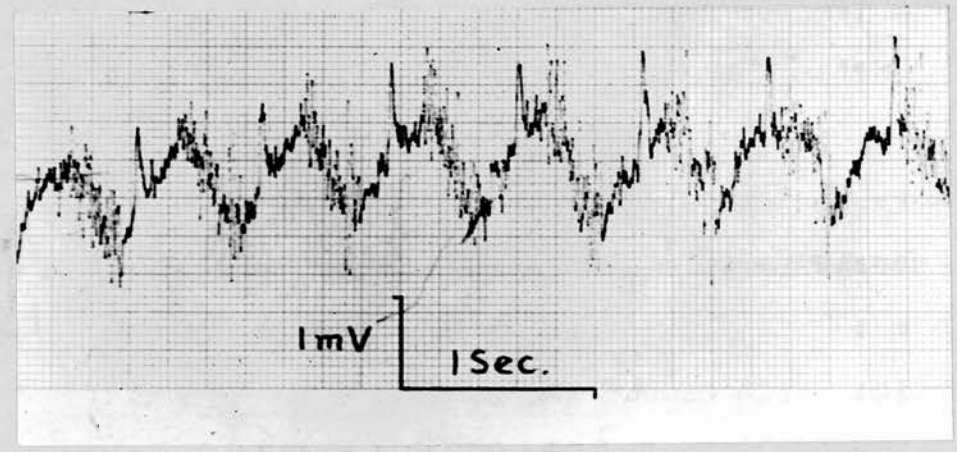


fig. 4. The exercise E.C.G. using conventional electrodes.

leads were used - one over the apex beat of the heart and one in the second intercostal space near the mid-line. The earth was attached to the skin near the xiphisternum. Using this arrangement of electrode positioning in combination with the differential amplifier, the unwanted muscle noise was reduced to a minimum. However, during exercise this did not overcome the problem of the low frequency responses produced by the movement of the electrodes themselves (fig. 4).

During the early stages of this study it was found that the conventional type of electrodes were most unsatisfactory for exercise purposes. Not only were they cumbersome, but considerable acceleration of the main body of the electrode was produced. Also, during a period of prolonged exertion which caused the subject wearing the electrodes to perspire, there was a great danger of losing contact between the electrode and the subject's skin. After experimenting with a variety of electrode shapes and fixing arrangements to attempt to overcome these difficulties, a completely new electrode was developed (Davies and Copland, 1964).

Each electrode consists of a length of 9 cm., 0.5 mm., 18/8 hard stainless steel wire sharpened at both ends and bent as shown in fig. 5. This provides a powerful spring action which comes to a positive stop just before the points meet. The electrode is clipped into the chest so that the points just penetrate the superficial layers of the skin, thus ensuring positive fixing in one place. It can be further

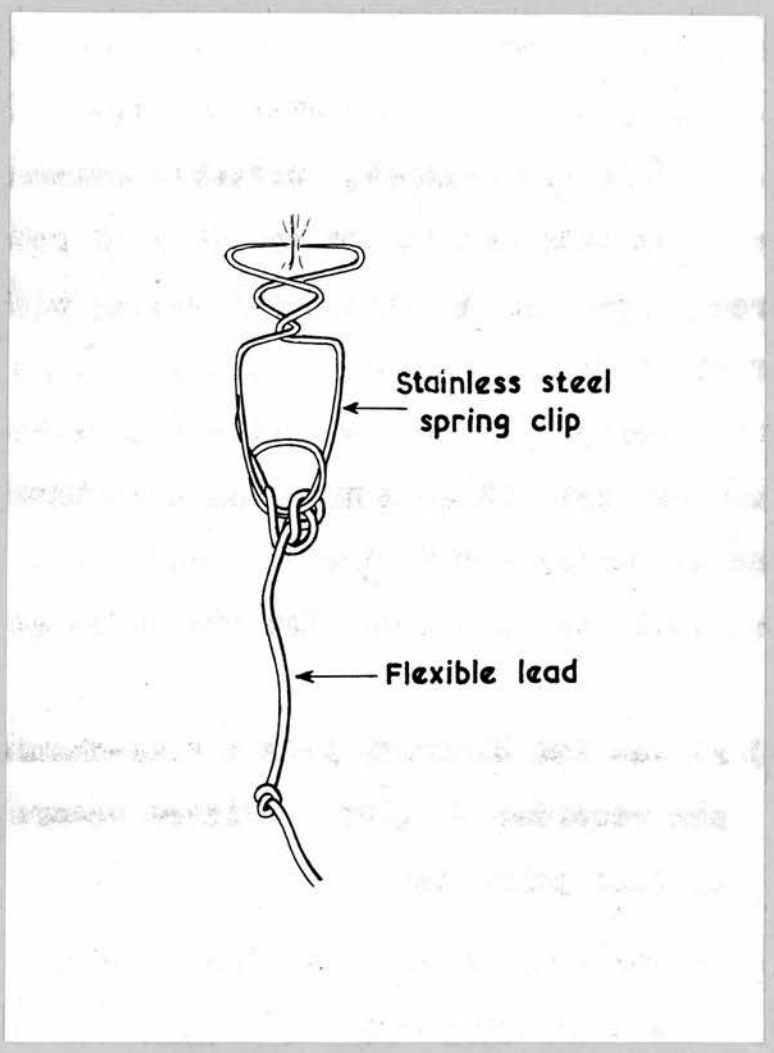


fig. 5. A new clip electrode used for displaying the E.C.G. during exercise. The points of the electrodes penetrate the superficial layers of skin and are stabilised in position with plastic adhesive strapping.

stabilised in position with plastic adhesive strapping. A satisfactory low impedance can be ensured if electrode jelly is smeared over the electrode site before attachment. The clip electrode is completely painless, provided that the points are sharp and they are not allowed to cross over during attachment. Reliable records of heart rate have been obtained in the presence of potential interference from the treadmill and during violent movements of the body while running at 7 m.p.h. up an 18% gradient. During the whole experimental series no subject complained of pain either during the attachment of the electrode or during the period of exercise.

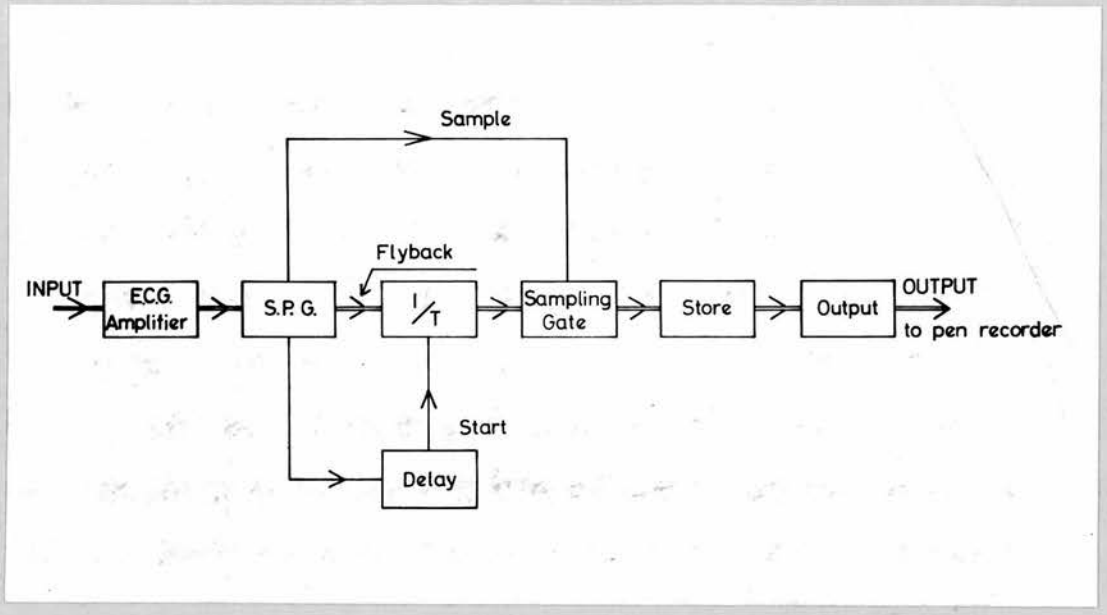
The resulting E.C.G. was treated in three different ways:-

(a) it was fed directly into a four-channel pen recorder to give a written record of each pulse beat;

(b) it was passed into one channel of an F.M. tape recorder;

(c) it was made to operate a linear instantaneous ratemeter.

This latter piece of apparatus was made especially for this study by Dr. J.M.M. Neilson of the Department of Medical



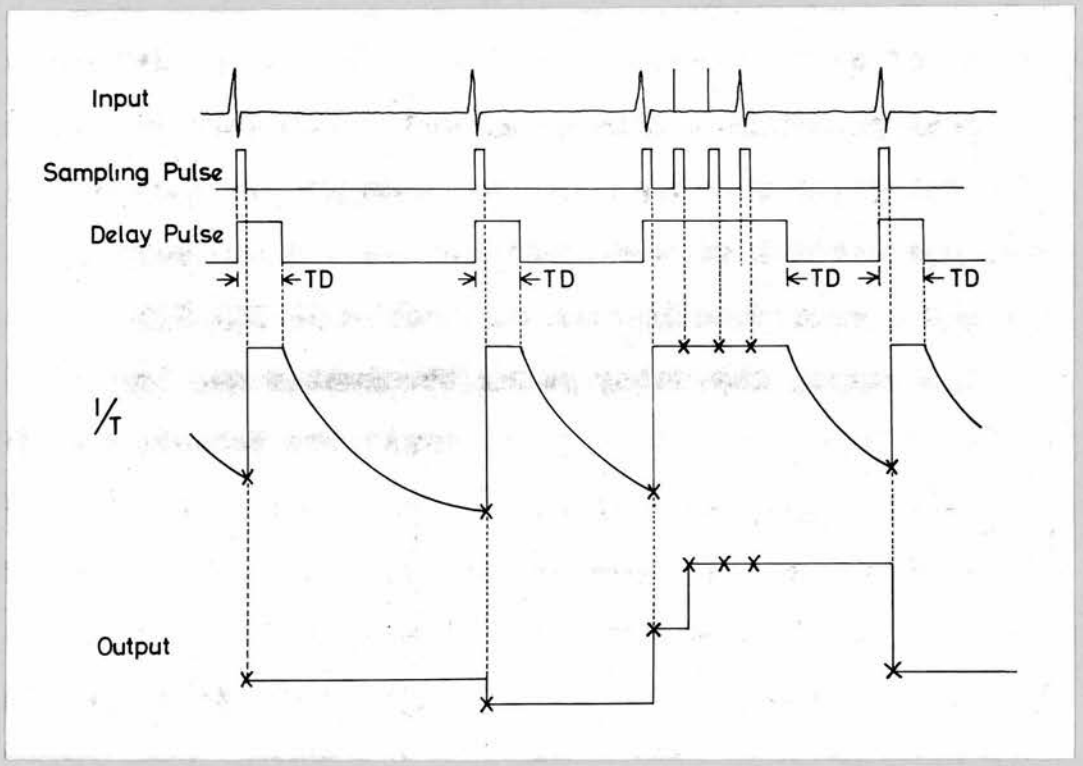


fig. 6(a). 6(b). **Block diagram of the rate meter circuit and some of the applied waveforms to show its operation. See text.**

Physics, Edinburgh. It is intended that the full circuit diagram will form the basis of a separate publication (Neilson, 1965). The function of the instrument is to produce an output voltage which at all times remains inversely proportional to its time interval between the last two input pulses, i.e. proportional to the instantaneous heart rate. Fig. 6a shows a block diagram of the arrangements of the ratemeter and fig. 6b some of the applied wave forms to show its operation. The trigger pulses from the output of the E.C.G. amplifier are used to fire a monostable circuit which produces a sampling pulse of about one millisecond in duration. Simultaneously, a delay pulse generator is triggered so that the start of the delay pulse coincides with that of the sampling pulse and the arrival of the input pulse. At the end of an interval corresponding to the period of the highest rate on the range, the delay pulse terminates and the falling edge of this pulse is used to start the hyperbolic run-down in the $^{I}/_{T}$ waveform generator. When the next input pulse arrives another sampling pulse is generated and another delay pulse started. This time the sampling pulse is used in the following way. The time scale of the hyperbolic run-down is such that even at its steepest part there is negligible change in its level during the sampling pulse. In this short interval a transistor sampling switch is closed, transferring the voltage of the $^{I}/_{T}$ waveform to a storage capacitor. At the end of the sampling pulse the switch opens, locking the sample in the store and initiating

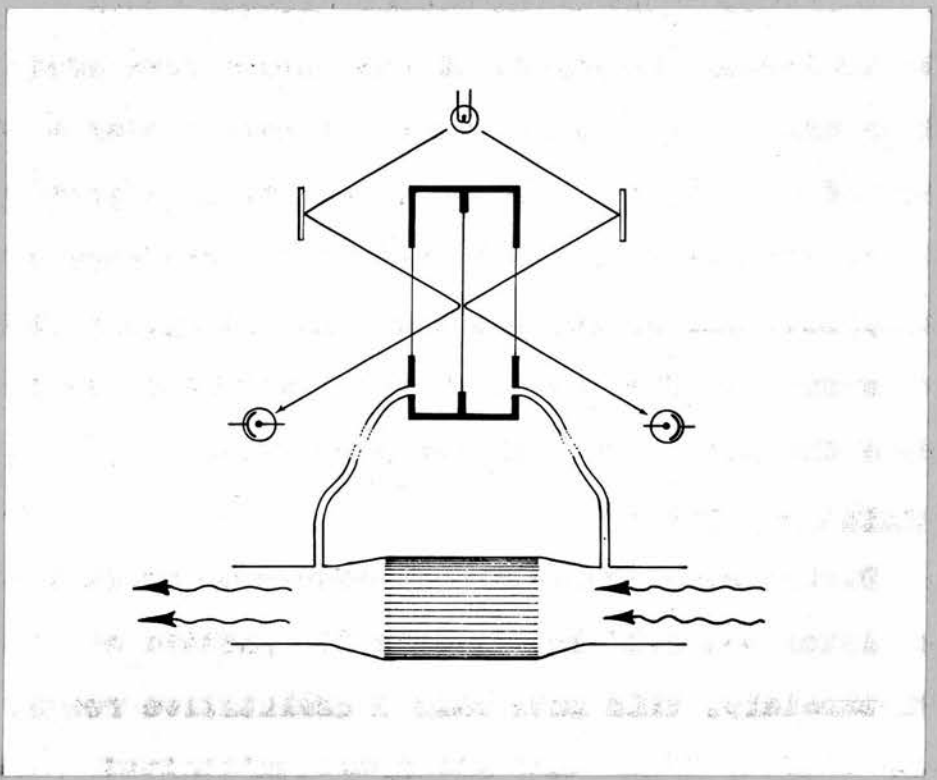


fig. 7. Diagrammatic representation of the Fleisch pneumotachograph screen and Greer micromanometer.

fly-back of the $^{I}/_{T}$ waveform.

The voltage on the storage capacitor is fed to the output stages of the instrument through a high impedance stage which has an input impedance sufficiently high to allow only a negligible change in the stored sample in a time corresponding to the longest period (i.e., the lowest rate covered). Linearity of the output rate scale was better than $\pm$ 1% of full-scale deflection over a working range of 0 - 200 beats/minute. Inputs at higher frequencies falling outside this range resulted in readings at the appropriate end of the scale so that ambiguous readings were avoided. The output of the instrument was fed to the second channel of the pen recorder (fig. 2).

Respiratory volume

During experiments at the beginning of this study a bead thermistor was used to indicate the pattern of breathing. Unfortunately, this gave only a qualitative record of respiration. If an expiration was maintained, for example, the recording was not steady, but fluctuated with the changing temperature of the cooling thermistor. A new method was developed using a Fleisch pneumotachograph screen (type 2) and a micromanometer (Greer, 1958). Expired air flows through a wide bore tube (fig. 7) past the screen. The screen essentially consists of a bunch of capillary tubes which ensures a streamlined flow of air through the resistance so formed. The careful design of the apparatus ensures that the pressure difference across the screen is proportional to the gas velocity, at least within a restricted range.

The back pressure produced by the screen is kept at a minimum, being only a few millimetres of water at the maximum velocity produced during exercise. The small dead space and low resistance of the apparatus enables the subject to breathe normally and without restriction.

The pressure signal is transformed into an electrical one by using a micromanometer (Greer, 1958). This instrument was chosen to provide stability, linearity and sensitivity, all of which are necessary if the output is to provide a satisfactory integrated signal. The pressure difference is applied to the opposite sides of a thin membrane and the resulting deflection is used to produce a differential focussing effect on the light from a common source onto two photo-cells in a bridge arrangement (fig. 7). The unbalanced voltage from the bridge is linearly proportional to the original pressure difference and a full scale sensitivity of only 3 cm. of water can be achieved with virtually no zero drift. Occasionally the velocity signal from the manometer was recorded directly on the pen recorder and F.M. tape system; the velocity signal was usually integrated in a Solartron operational amplifier to produce a signal proportional to the volume of gas which had crossed the screen at any instant. This volume signal was then monitored on the pen recorder and recorded on magnetic tape along with the E.C.G. and pressure signals.

Respiratory pressures

(i) Intrathoracic pressure

This was measured by means of an intraoesophageal

balloon (Mead and Whittenberger, 1953) which was passed through the naso-pharynx into the middle third of the oesophagus (Milic-Emili, et al., 1964) and a Greer micromanometer modified to give 100 cm. H_2O full scale reading.

(ii) Intrapulmonary pressure

This was measured using a Statham pressure gauge in combination with the bridge circuit and amplifier in the Devices pen recorder. The Statham gauge was attached to the side tubing of the Fleisch pneumotachograph screen by means of a "T" piece arrangement so that any change in pressure or volume could be recorded simultaneously.

The pressure signals from the Greer manometer and the bridge amplifier were monitored and recorded on the F.M. channels of the tape recorder in the usual way (fig. 2).

Calibration

The ratemeter was calibrated from a standard signal generator (Solartron Ltd.). It is linear throughout its range and has an accuracy of $\pm$ 1%. The pneumotachograph was calibrated by means of a Starling respiratory pump.

A conventional water manometer was used for calibrating the Greer manometers in experiments where intrathoracic and intrapulmonary pressures were measured. All systems were calibrated before and after the actual experimental period and they were recorded on magnetic tape.

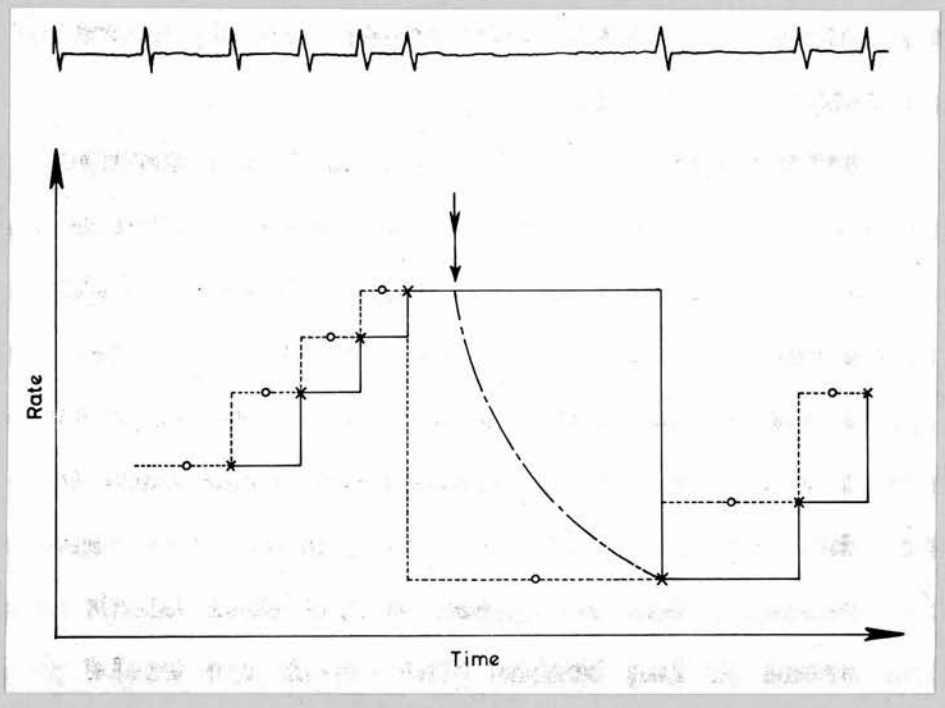


fig. 8. The relationship between individual heart beats and instantaneous rate. Note that the pen represented by the black line can only take a position corresponding to the instantaneous rate when that rate has been defined, i.e. at the next pulse.

Analysis of the records

For analysis of the records, the parts of the tapes containing the responses were replayed from the tape recorder into the pen recorder using a faster paper speed and a more open scale for the heart-rate channels (fig. 9). Measurements were then made manually from these recordings and average responses were worked out by means of a desk calculating machine.

Before attempting to interpret the original records in this thesis, the exact relationship between the individual pulses and the line representing the instantaneous rate drawn by the pen recorder must be considered. Fig. 8 shows that the pen can only take up a new position corresponding to the instantaneous rate when that rate has been defined, i.e. at the next pulse. The resulting trace will resemble the one given by the full black line. The line seems to lag behind that which one would perhaps like to draw (dotted line) if the rate were plotted manually. Achievement of this presentation electronically would be impossible. But a close compromise to the desired presentation can be achieved by allowing the pen to fall as soon as the time interval for the previous pulse has elapsed. Provided that it does not fall below the reciprocal of this time, a trace as shown by the chain dotted line is achieved. This presentation was first suggested by Andrew and Roberts (1954) and it has been used throughout this study. Fig. 9 shows an actual experimental record played out at a fast speed and the exact relationship between the individual

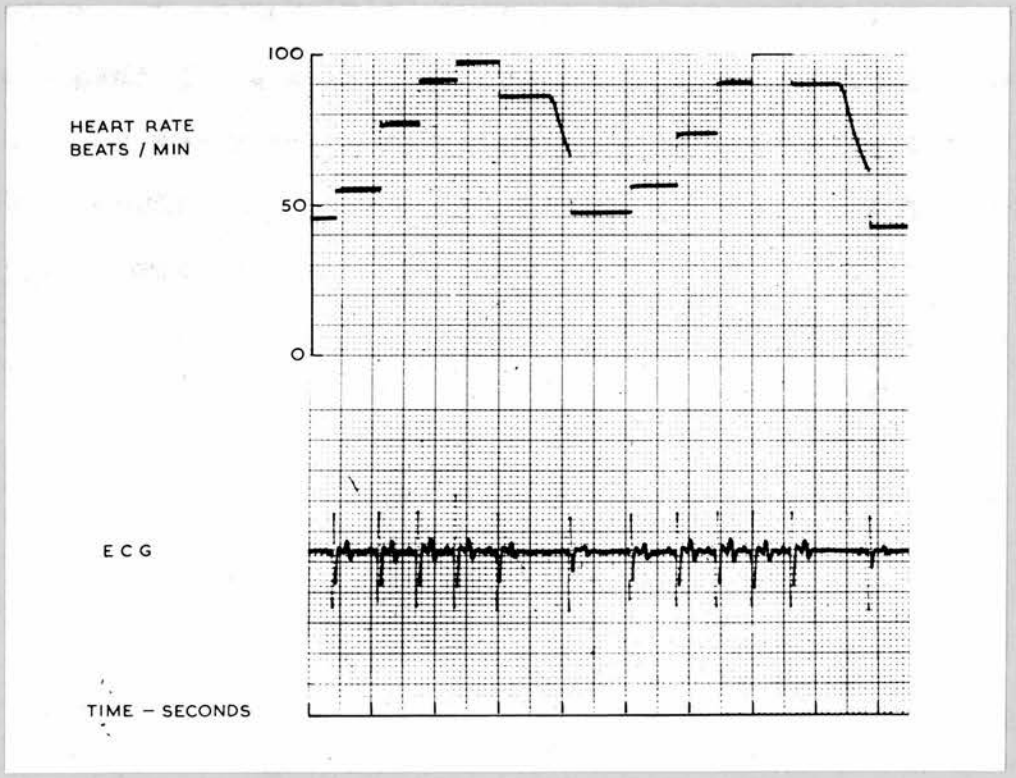


fig. 9. An experimental record played out at fast paper speed showing the exact relationship between individual pulses and instantaneous rate. This paper speed was used for the manual analysis of the individual responses.

pulses and instantaneous rate can be seen. But it should be remembered that a line joining the points on a graph or record of this nature is only an aid to visual interpretation and the actual rate between the points remains undefined.

The ratemeter-pen recorder combination was calibrated at the beginning of each replay session. By this means, it was estimated that the residual errors due to the nonlinearity of the system and interpolation between calibration points were reduced to a minimum and were less than one beat per minute.

TABLE II.

Response of the heart rate to inspiration.

	No. of Observations	heart rate - beats		
		range	mean	S.D.
Amplitude	97	4 - 33	15.90	6.68
Overshoot	97	-14 - +13	-1.40	3.74

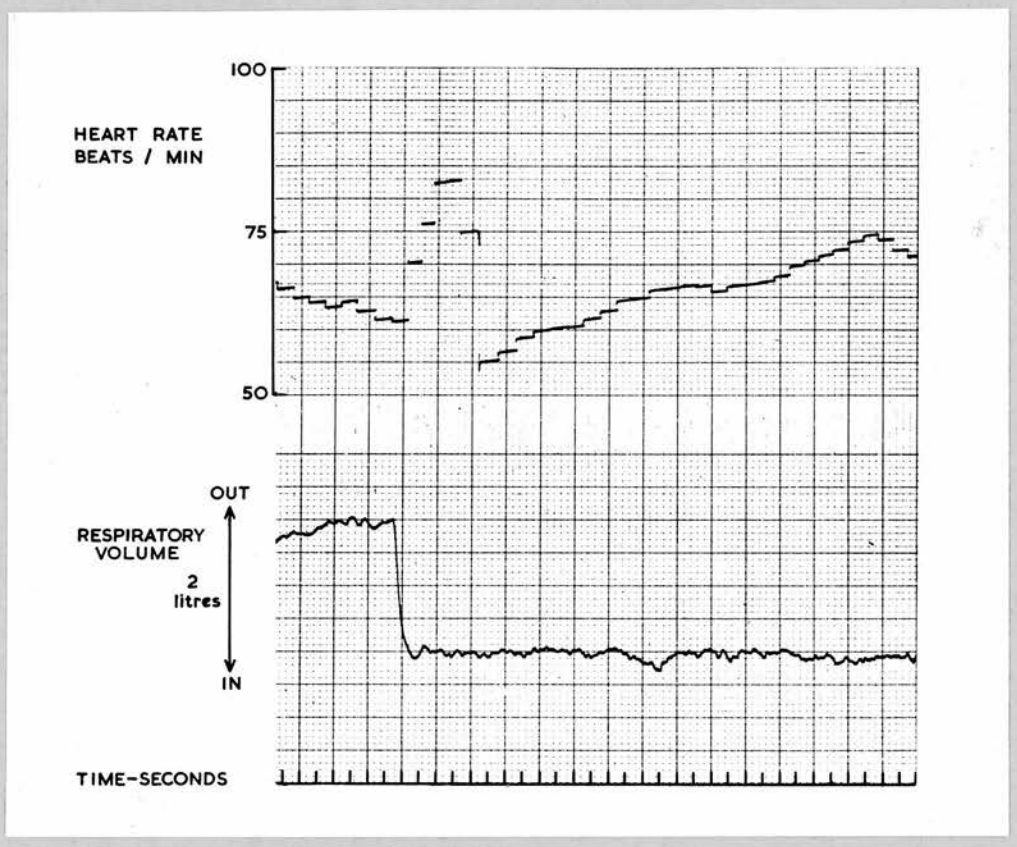


fig. 10. An experimental record taken during the performance of a step inspiration.

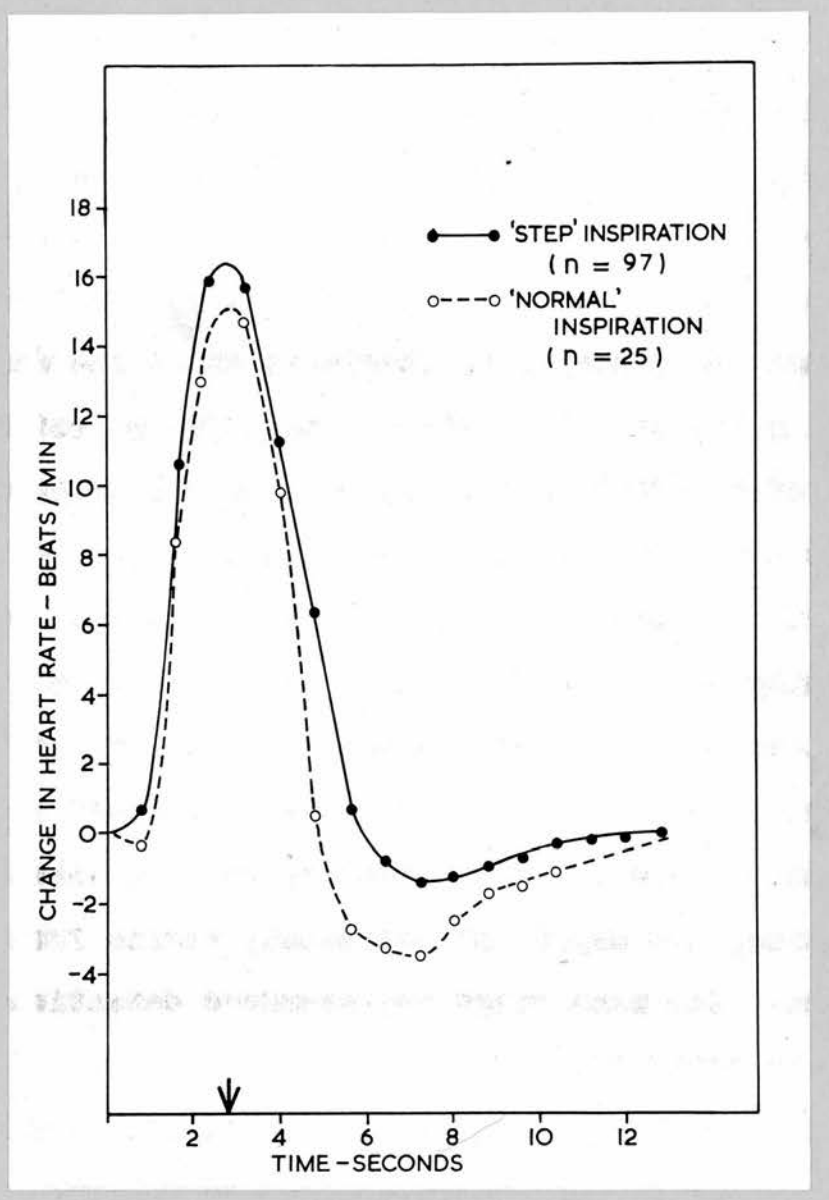


fig. 11. The averaged response of the heart rate to 97 fast ("step") and 25 "normal" inspirations performed by the 10 subjects throughout the experimental period. The arrow marks the time taken to reach maximum tachycardia (2.8 seconds).

1.4. Results

1.4.1. The effect of inspiration on the heart rate

The change in heart rate produced by a fast inspiration can be seen from figs. 10 and 11. Fig. 11 shows the averaged response of 97 inspirations performed by different subjects throughout the experimental period. The reflex response has a very characteristic shape and was similar in all subjects. The delay which occurred before the onset of the fast rise in heart rate was never more than one second. Maximum tachycardia was reached within a time interval of three heart beats (2.8 seconds). During the following six beats the heart rate decelerated crossing the zero line at 5.5 seconds after the onset of inspiration. Following this decelerating phase, the heart rate usually returned gradually to its initial resting value. The amplitude, and degree of overshoot, varied from subject to subject. The mean range and standard deviation figures are given in table II.

The duration of the biphasic response compares favourably with that reported by Clynes. The main difference between the two sets of results is the actual magnitude of the response and degree of overshoot. From the published figures of Clynes the magnitude and degree of overshoot are shown to be of the order of 50 and 35 beats/min. respectively, compared with 15.9 ± 1.38 and 1.40 ± 0.78 found in this study.

The difference in magnitude could be accounted for in a number of ways. The postures adopted by the experimental

subjects were different in the two studies: supine compared with sitting in this investigation. Reference to fig. 12a shows that there is a tendency for the mean amplitude of the response to increase when a subject is transferred from sitting to the lying down position, but whether this factor alone could account for large (34 beat) differences is doubtful. A more plausible explanation could possibly be found in terms of the different volumes and rates at which air was taken into the lungs in the two studies. The only way to settle this point would be to compare the volume records during the performance of the inspiratory manoeuvres in each experiment. This is, however, not possible, because volume as such was not measured in Clynes' investigation. He used a rubber tube filled with powdered graphite passed around the chest to monitor respiration. This method merely gives a record of the change in thoracic circumference during inspiration which cannot necessarily be equated with direct changes in lung volume.

The large overshoot in heart rate is more difficult to account for; the results of this investigation indicate that the supine position diminishes rather than enhances the observed overshoot (fig. 12.). It could possibly arise from the different methods used for analysis: the manual method compared with on-line digital computer of average transients (C.A.T.), though this would seem most unlikely. In Clynes' paper no mention was made of the precautions taken to ensure that the subject's glottis remained open

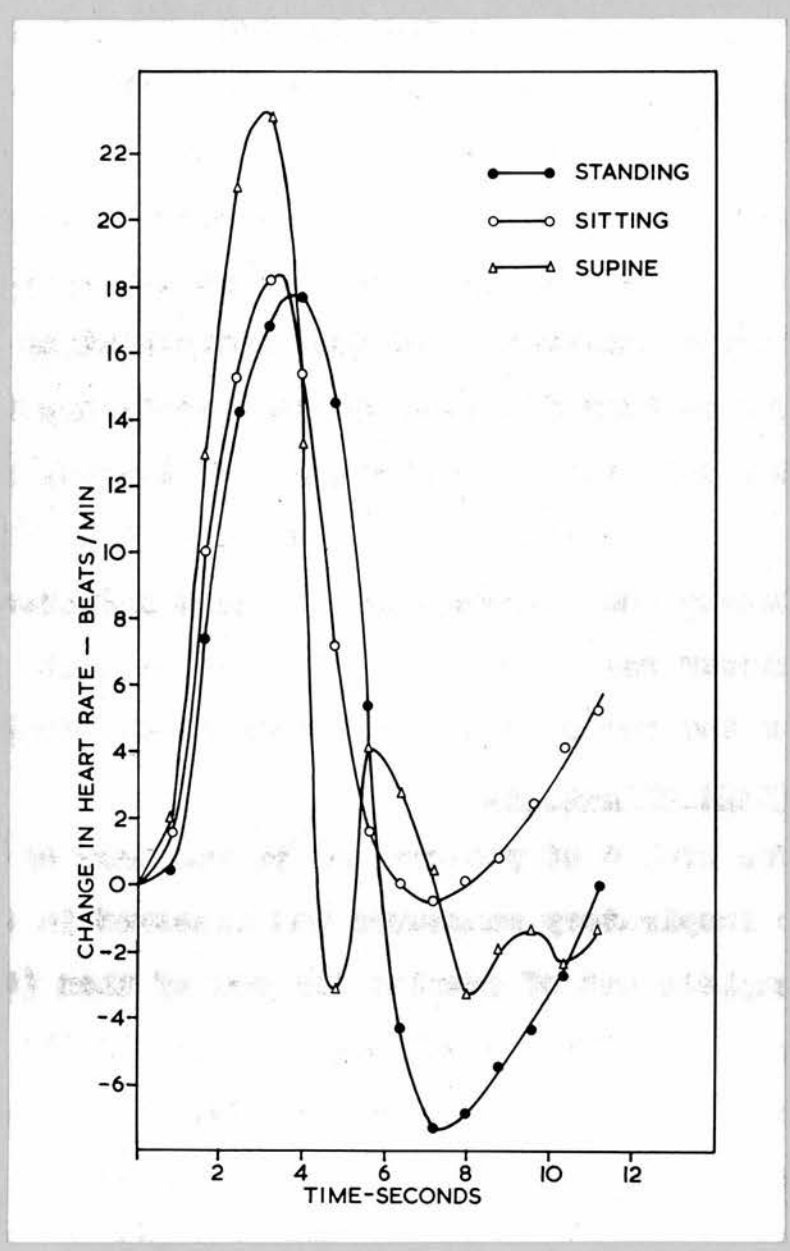


fig. 12a. The effect of posture on the response of the heart rate to step inspiration in one subject (n = 6). He was measured in the standing, sitting and supine positions.

throughout the whole manoeuvre. In this study it was found to be of paramount importance. When left to perform the manoeuvre of his own accord there was always a natural tendency for the subject to close his glottis and this usually gave rise to unwanted pressure effects and a larger deceleratory phase (fig. 1). Nevertheless, even during the preliminary experiments of this investigation in which the subjects performed the manoeuvre without specific instructions from the experimenter regarding the glottis, an overshoot as great as 35 beats/min. was never recorded. It is perhaps unfortunate that Clynes does not give sufficient data to make closer comparison possible and the large discrepancy between the two studies more readily explicable.

The effect of posture

The effect of posture on the response of the heart to a step inspiratory manoeuvre was measured in two subjects. The complete set of results for one of them (E.J.W.) is shown in fig. 12. The subject was measured in the standing, sitting, and supine (with feet raised 9" from the ground) positions. It would seem that the effect of lowering the body position from the standing to supine position was to increase the magnitude of the response and to reduce the duration of the deceleratory phase. Maximum bradycardia was reached in 4.8 secs. (3 beats) in the supine compared with 7.2 secs. (5 beats) in the sitting and standing positions. The sharp rise and fall of the heart rate following the biphasic inspiratory transient on the supine position (fig.12.) was

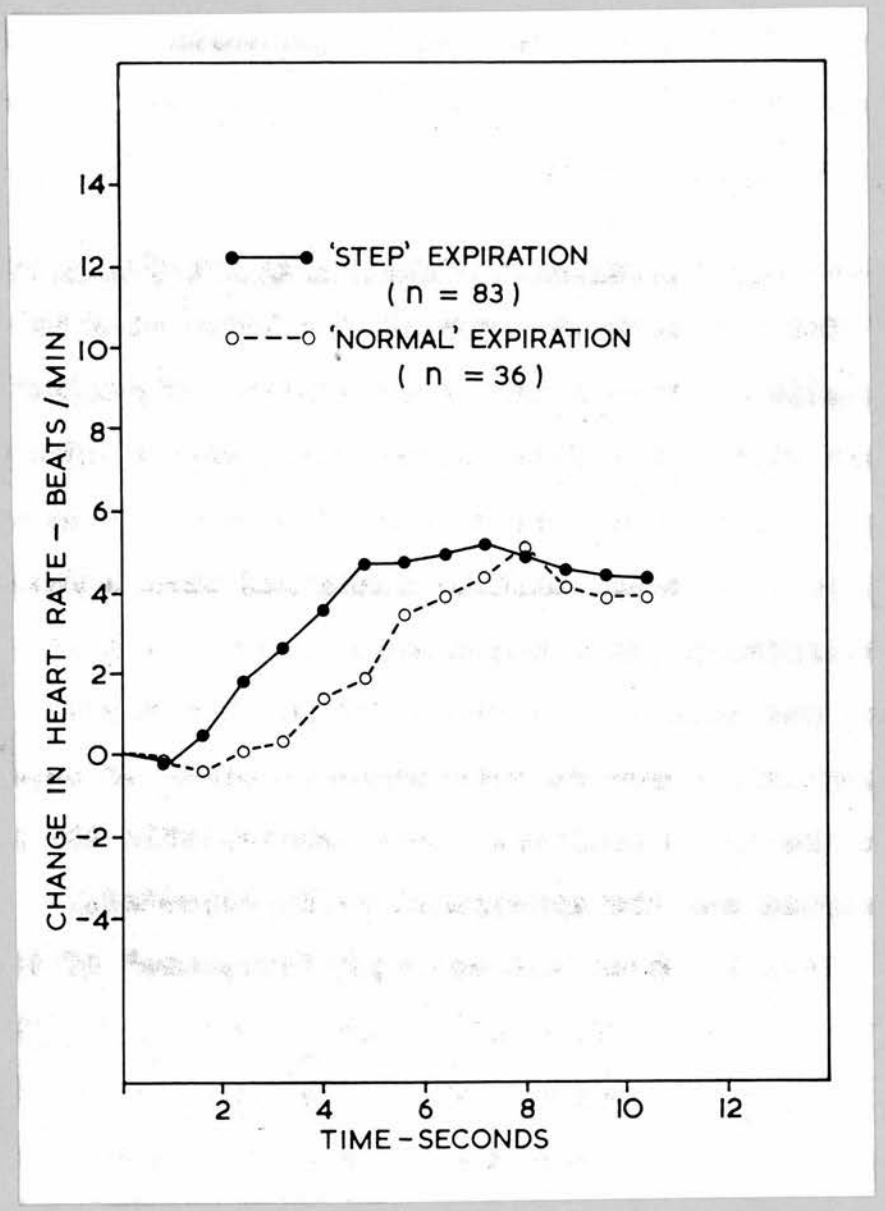


fig. 13. The averaged response of the heart rate to 87 fast ("step") and 36 "normal" expirations performed by the ten subjects throughout the experimental period.

a consistent finding in both subjects and following the performance of some manoeuvres it was often possible to identify a definite oscillatory pattern. The heart gradually returning to its resting value is a series of waves of decreasing amplitude.

1.4.2. The effect of expiration on the heart rate

The averaged response of the heart rate to a step expiration varied widely from subject to subject and often varied within the same subject from day to day. In most cases, unlike the results for step inspiration it was difficult to judge whether there had been a response at all. Most subjects found the manoeuvre difficult to perform and there was always a tendency for some to breathe in slightly immediately prior to expiration in order to expel the air from the lungs rapidly. This necessitated the results being discarded and the experiment being repeated.

Fig. 13 shows the averaged "response" of the heart rate to 87 fast expirations. The heart exhibits a small rise in rate and a tendency to remain elevated above the resting base-line. The response could be modified in several ways: if the subject performed the manoeuvre from the inspiratory breath held position, expiration invariably produced a fall in heart rate followed by a rise - the effect of posture was to increase this initial drop in rate; and by allowing the subject to breathe out quickly, but to maintain a relaxed and comfortable body position in order to avoid excessive contraction of the abdominal muscles the "response" was

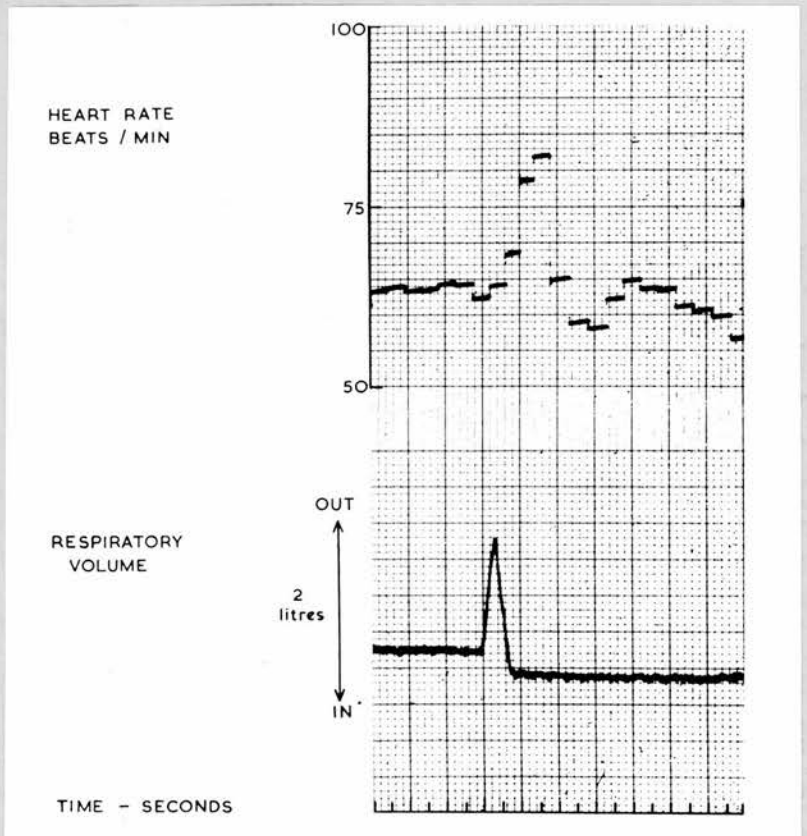


fig. 14a. Record of the heart rate response due to positive "impulse" breath. Note evidence of slight delay of the heart rate response compared with the negative impulse.

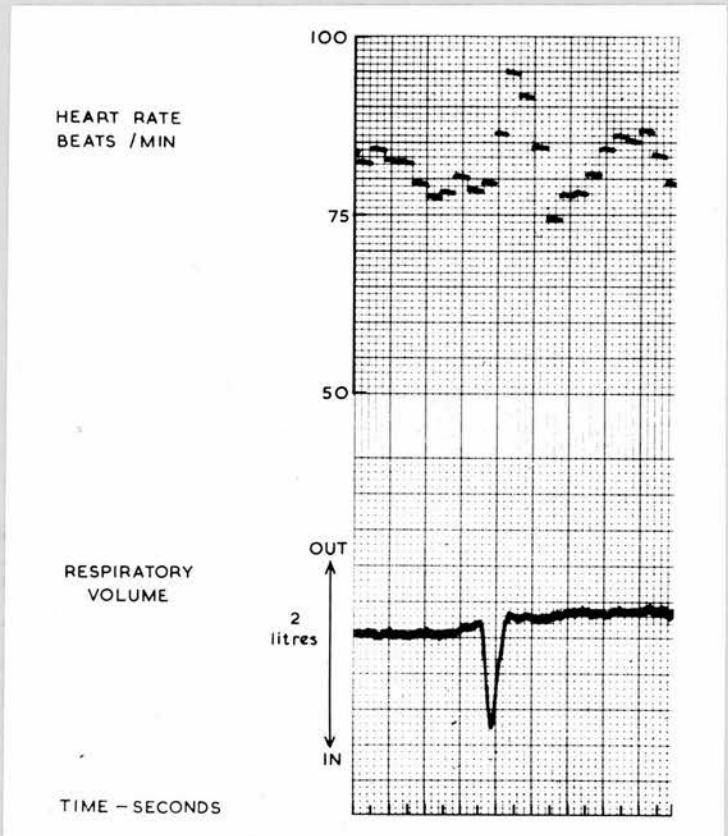


fig. 14b. The heart rate transient due to negative impulse breath.

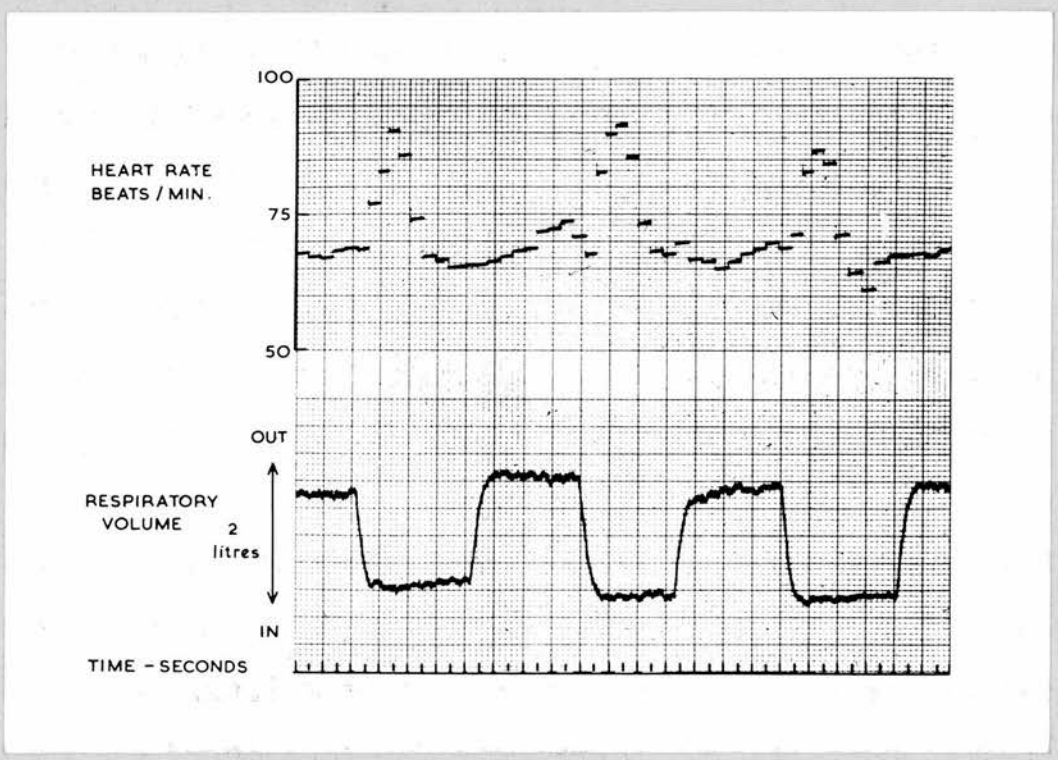


fig. 15. The response of the heart rate to "pulse" respiration. Note that expiratory edge of the pulse has little or no effect on the heart rate.

often reduced and delayed. These results suggested that there might be no true response to expiration, provided the manoeuvre was not prolonged. Consideration of the final three manoeuvres performed by all subjects would tend to confirm this view.

"Impulse and "pulse" respiration

Negative and positive "impulses" (Clynes, 1961) were performed as follows: each subject was asked to breathe "out-in" or "in-out" and quickly hold the breath in a manner previously described. The results for one subject are shown in fig. 14. Both negative (out-in) and positive (in-out) shows a similar biphasic response to that described for a single fast inspiration. Provided the subjects either inhaled or exhaled a similar volume of air at the same rate there was little difference between the negative and positive impulses except that there is suggestion of slight delay occurring before the onset of the former response (fig. 14b). This becomes more evident if the subject is allowed to breathe in a series of pulse respirations of increasing width (fig. 15). The reflex response of heart rate is clearly not triggered by the negative (expiratory) edge of the pulse. The change in heart rate observed is almost entirely due to inspiration: expiration having very little effect on the heart rate.

This can be further illustrated by considering the effect of (1) breath-holding following a piece of mild exercise and (2) breathing at different respiratory frequencies, on the heart rate.

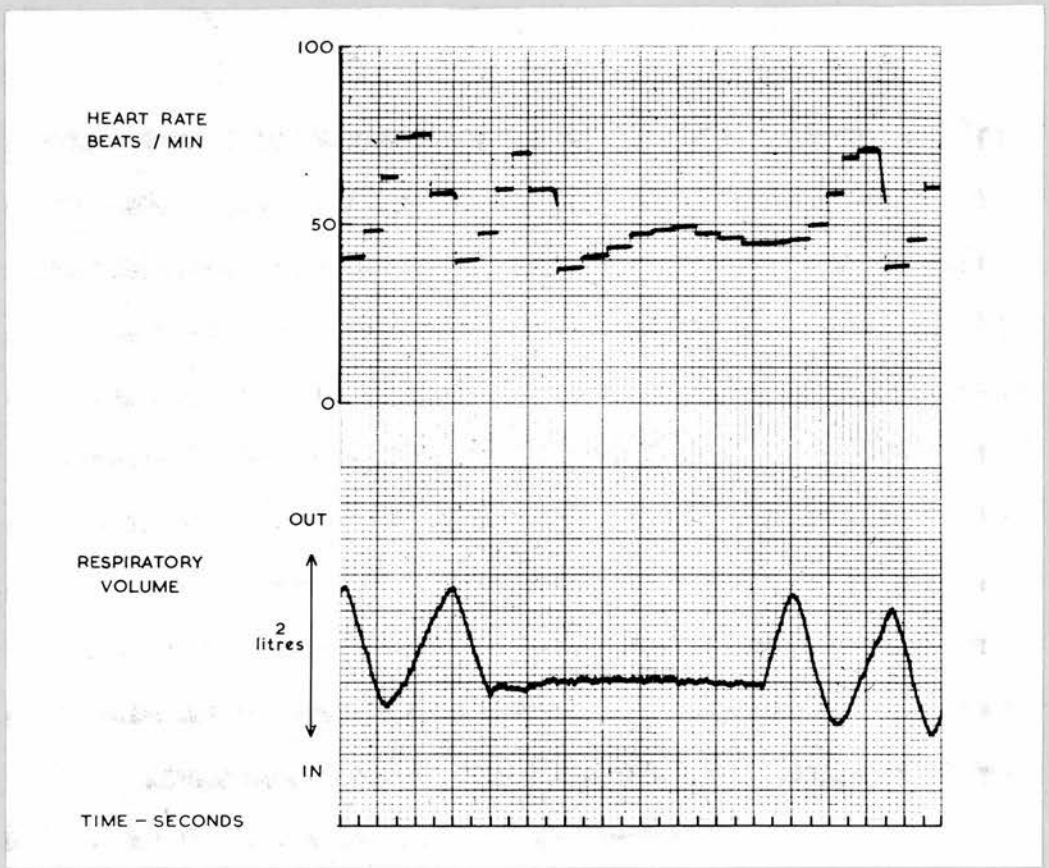
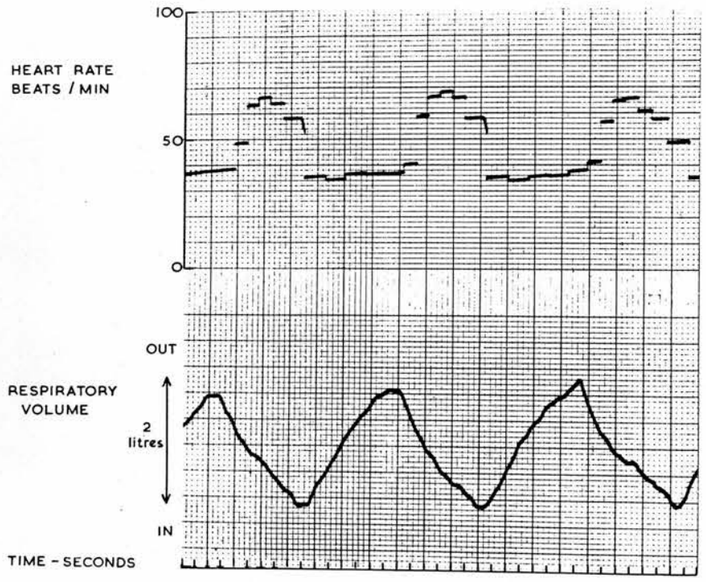
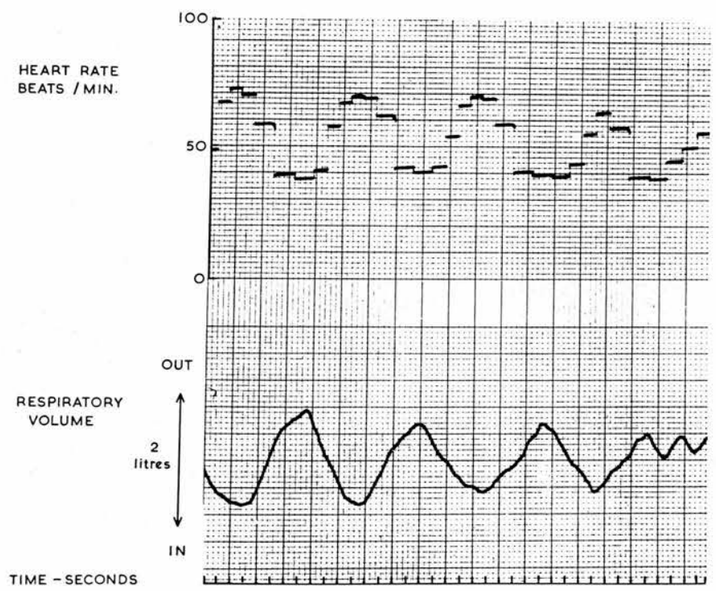


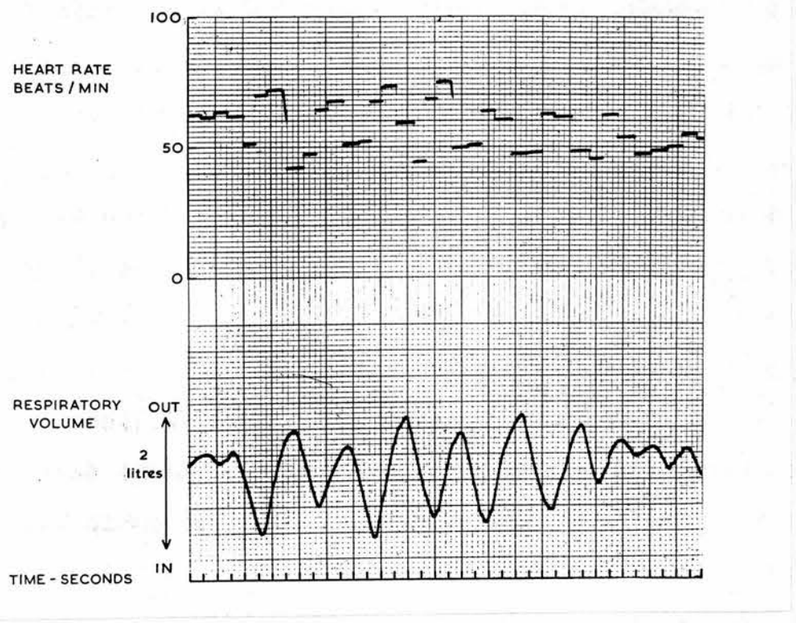
fig. 16. Record of heart rate and respiratory volume during a breath-holding experiment. At the beginning of the manoeuvre the heart rate transient due to inspiration completes itself, then sinus arrhythmia disappears during the breath-holding period and does not reappear until the onset of the next inspiration. Note that the release of breath (expiration) has no effect on the heart rate.

At the onset of the breath-holding period (fig. 16) the heart rate transient due to inspiration completes itself in a manner previously described (cf. fig. 10). This is followed by a period when the heart rate remains constant during the remainder of the apnoeic period. Upon the release of breath the heart rate is completely unaffected by the expiratory effort. No change in heart rate is observed until the onset of the next inspiration. Similarly, if a subject is made to breathe at different respiratory rates it can be seen from fig. 17 that at the higher respiratory frequencies considerable destructive interference takes place, due to the fact that there is insufficient time for the inspiratory heart rate responses to complete themselves, but as the frequency decreases the responses become more and more separated. The lowest respiratory rate heart rate wave due to inspiration is clearly defined by an expiratory period during which the heart rate remains constant.

Thus, in contrast to the findings of Clynes (1961) the rise and fall of heart rate which accompanies respiration at rest would seem to be determined solely by inspiration. In particular there is no evidence to suggest that the heart rate control system is affected by two separate inspiratory and expiratory reflexes. Considered in this light, Manzotti's conclusion drawn from the results of breath-holding experiments at rest, that respiration precedes the heart response by five seconds, is erroneous. He failed to appreciate the biphasic nature of the heart rate response to inspiration.







ig. 17. The effect on the heart rate of different breathing frequencies: a) 4 breaths/min. b) 8 breaths/min. c) 16 breaths/min. As respiratory frequency increases the heart rate transients due to inspiration come closer together at 16 breaths/min. and destructive interference takes place.

If his subjects had been asked to hold their breath at the end of an expiratory effort, the results would have been quite different.

The work of Angelone and Coulter (1964), too, is made more meaningful: The difference in phase angle between heart rate and respiration is merely the result of the three-second delay which occurs before the heart rate begins to decelerate after the onset of inspiration. If we assume that both the fluctuation in heart rate and respiration can best be represented by a sine-wave, and given a standard delay of three seconds, then at five and ten breaths/min. the heart rate will be 90^{o} and 180^{o} "out of phase" with respiration, respectively. As the respiratory rate increases beyond 15/min. the inspiratory waveforms will become superimposed to produce a distorted phase relationship and irregular fluctuations of the heart rate of decreased amplitude (fig. 17c). Thus, the relationship between phase angle and amplitude at various respiratory frequencies as described by Angelone, can be constructed.

1.5. Discussion

The results offer a new description of sinus arrhythmia in man. They show that the relationship between heart rate and respiration is governed mainly by the biphasic nature of the inspiratory heart rate transient which has an amplitude of approximately 16 beats/min. and a duration of 13 seconds. No evidence was found to suggest that the heart rate control system was affected by two separate inspiratory and expiratory reflexes. Expiration had little or no effect on the heart rate. Thus, under normal resting conditions the basic pattern of heart rate fluctuations attributable to sinus arrhythmia will depend on respiratory frequency, only at low breathing rates will a clear rise and fall of heart rate be seen. At higher frequencies (above 15/min.) superposition of the inspiratory transients will take place to give rise to various heart rate patterns. Unfortunately, the underlying mechanisms which might be responsible for these observed changes of heart rate with respiration are less clear and at the moment speculative.

In animals, as we have seen, sinus arrhythmia has been variously attributed to: (1) afferent impulses from stretch receptors within the lungs affecting the vagal centre directly and indirectly via the respiratory centres; (2) haemodynamic factors, i.e. changes of blood pressure accompanying respiration either through pressure receptors on the venous side or the left side of the heart; and (3) central influences by irradiation of impulses from the respiratory to the vasomotor centre. How far are these views tenable in man?

1. Afferent impulses from the lungs

Manzotti (1958) dismisses the possibility of afferent impulses on the grounds that a delay of five seconds between respiration and the ensuing heart rate changes was too long to justify a stretch receptor mechanism. Clearly, from the results of this investigation his basic premise was incorrect. The delay between the onset of inspiration and the biphasic heart rate response is less than one second which is in agreement with the figures quoted by Adrian (1933) and Pitts (1942) for the pulmonary reflex pathway delay in experimental animals. Clynes, on the other hand, dismisses factors 1 and 2 and claims that "Sinus arrhythmia is initiated by a stretch receptor located within the chest and is not primarily caused by haemodynamic factors or central influences."

The Clynes model, which involves a doubly differentiating unidirectional transfer function between respiratory and vagus inhibition is based on his observation that the responses to inspiration and expiration are biphasic and in the same direction. Though his model simulates actual results obtained on human subjects reasonably satisfactorily, it would seem difficult to support it on experimental grounds from the findings of this study. It must be remembered that, though a model may give accurate simulation of actual results, it cannot prove that the solution given is the correct one. It merely indicates that it is one possible (but not unique) solution. One of the differentiates may be due to a stretch receptor; it could equally be due to any other factor which

depends on the rate of expansion of the lungs. Certainly, the results do not rule out a stretch receptor being involved at least during inspiration, but it would seem doubtful if it is the only factor responsible for the observed changes in heart rate. No respiratory heart rate control system based purely on a stretch receptor mechanism could adequately account for the effects of either posture or exercise (see page 24) on the changes of heart rate associated with respiration.

2. Haemodynamic factors

Clynes' case against haemodynamic factors being involved rests on the observation that the heart rate response to "negative" (out-in) impulse is of similar shape, but greater in magnitude compared with a single inspiratory transient, while "blood distribution change is likely to be less, since out-in ends and starts in the same position and is quite rapid." His argument would appear to be that the lungs inflate and deflate before blood had time to move into the pulmonary circulation. In terms of known haemodynamic responses to sudden lung inflation this is simply not acceptable. Heinbecker (1927), Daly (1930), Trimby and Nicholson (1940) and Cahoon et al. (1941), among many others, have shown that though a sudden decrease in intrathoracic pressure favours the inflow of blood to the heart, the concomitant rapid expansion of the lungs is more than adequate to accommodate the increased volume of blood from the right ventricle. Thus, an increment of blood may be withheld from the left ventricle, resulting in an immediate drop in aortic pressure (Hamilton et al., 1936; and Lawson et al., 1946). This fall in blood pressure has

been shown to occur at the very onset of a fast inspiration and thus, contrary to Clynes, it could be argued that this could give rise to an immediate increase in heart rate. Further, the rapid drop in heart rate which follows the initial response with a delay of 2.8 seconds (three heart beats) could result from a delayed rise in aortic blood pressure as the increased venous return facilitated by inspiration traverses the pulmonary circulation and arrives at the left side of the heart. Fig. 18 shows a typical result of a series of experiments performed on five subjects in which an attempt was made to simulate a sudden increase in venous return by asking them to release suddenly from a voluntarily-held positive pressure effort. It will be noted that following the release of the exertion the time delay before the expected abrupt fall in heart rate caused by blood reaching the left side of the heart is observed, is precisely the same order of magnitude as that reported for a normal inspiration held (cf. figs. 10 and 11) and in close agreement with work reported by Visscher et al. (1924). They showed that in dogs during normal lung inflation and clamping experiments in which venous return was occluded and then released suddenly, that the effect of increased venous return was shown on the left side of the heart by an approximately similar three-second (three heart beats) time lag.

Thus, the known effects of blood pressure changes which accompany respiratory movements and which depend on the expansion of the pulmonary vascular bed (i.e., rate of stretch of the lungs) could at least in part account for the inspira-

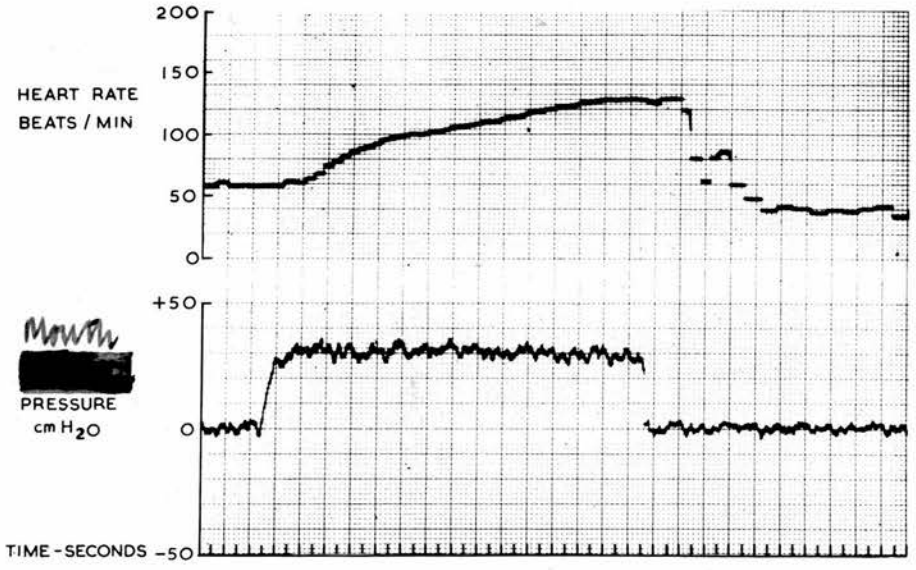


fig. 18. The heart rate (above) and ~~intra-pulmonary~~ Mouth pressure (below) during positive pressure breath-holding experiments.

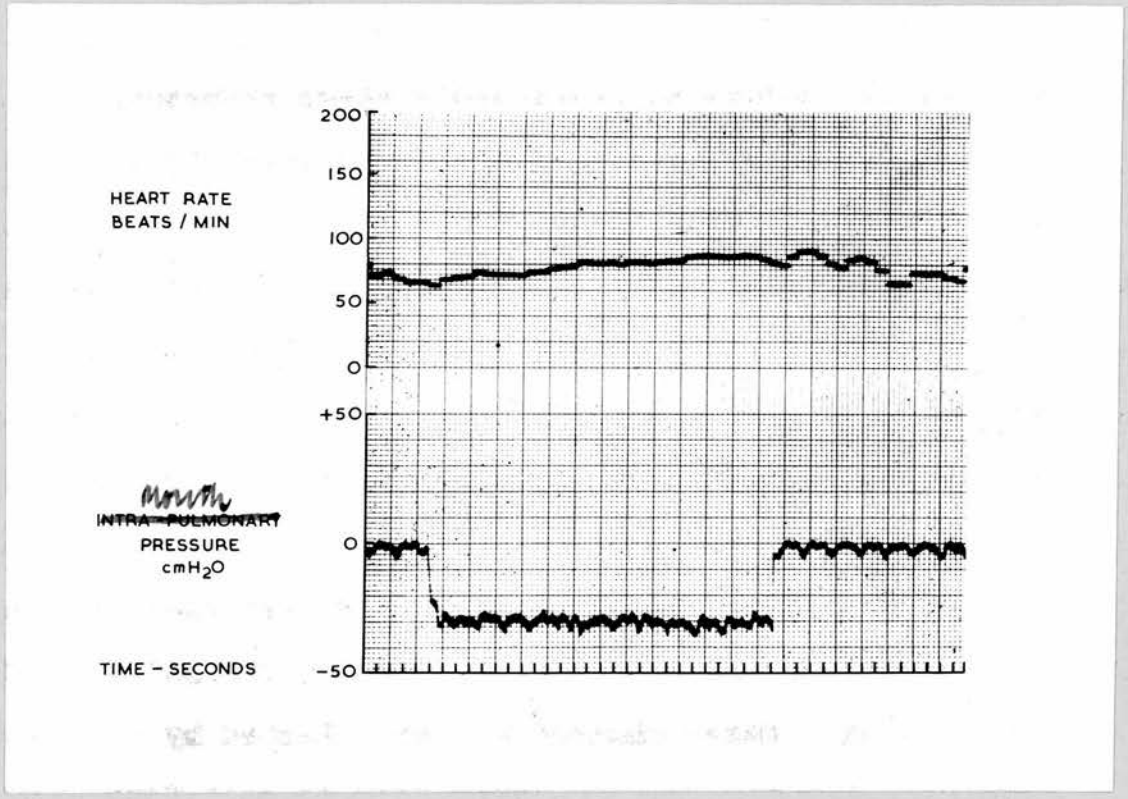


fig. 19. The heart rate and ~~intra-pulmonary~~ Mouth pressure during negative pressure breath-holding.

tory changes in heart rate and from the results of this investigation could equally well be proposed as a factor in the respiratory heart rate control system.

Central factors

In the intact human it is difficult to design an experiment to discover the exact contribution, if any, of central factors to respiratory sinus arrhythmia. Certainly, in the absence of lung movement during negative static (fig. 19) and normal breath-holding (fig. 16) no rise or fall of heart rate which could be correlated with respiration. These observations do not necessarily rule out completely the fact that impulses of central origin might be present (see Chapter 2), but they do suggest that if present their contribution must be small.

In summary, therefore, it may be said that the respiratory effect on the heart rate is mainly brought about by inspiration. These changes may be effected by a stretch receptor, but the results would seem to call for a more elaborate theory of the mechanism underlying sinus arrhythmia involving at least blood flow distribution changes within the pulmonary circuit and possibly the stimulation of vasoreceptor afferents situated on the left side of the heart.

CHAPTER 2

The recovery heart rate

2.1. Physiological background

The relationship of the heart rate to respiration as previously outlined in Chapter 1 affords a new description of sinus arrhythmia in man and forms the basis of the second part of this investigation which is concerned with the oscillations in the recovery heart rate as first reported by Lamb (1963) Having noted the publication of his results, a preliminary investigation of the heart rate pattern in forty-four subjects grouped according to age, sex and fitness following the performance of a standard exercise was undertaken. Analysis of the results revealed that, although moderately large fluctuations in heart rate did occur in most, but not all, subjects, they bore no apparent relationship to any of the above variables and were most commonly associated with respiration (Davies, Durnin and Neilson, 1963 - unpublished results). This was particularly so if a short burst of exercise was given. It was therefore suggested, contrary to Lamb, that the phenomenon of recovery cardiac oscillation might be an exaggerated form of sinus arrhythmia (Davies and Neilson, 1965).

The difficulty of firmly establishing this theory was, at the time of the experiments, that the precise relationship of heart rate to respiration under standard

conditions of rest was not known. This has now been established and it will now be shown that not only is the time course and magnitude of the observed oscillations in accord with a theory based on an underlying respiratory mechanism, but the phenomenon is frequency-dependent and obliterated by factors which are known to decrease sinus arrhythmia in man.

2.2. Procedure

The ten subjects form part of the previous investigation at rest and details of their age, sex, height and weight have been given in table I on page 10. The subjects reported to the laboratory, usually after a light breakfast or lunch, and were asked to rest quietly seated on a chair which was placed on the treadmill whilst the necessary electrodes and pneumotachograph screens were attached. Following this period the instrumentation was checked and records of the heart rate and respiratory pattern were taken. No attempt was made to gain absolute basal conditions. As soon as heart rate and respiration had been judged to have settled down and remained constant for a period of 15-20 minutes the subject was asked to stand and the chair was removed. A count-down in seconds was given and the treadmill started at zero time. The subjects ran for one minute up a 5% gradient and recovered standing for five minutes. The subjects then rested sitting down for a further twenty minutes or until the heart rate was within five beats of its previous resting value, whichever was the sooner. The whole exercise procedure was then repeated again.

In addition, one subject, C.J.F., was studied extensively on several different occasions, both on the treadmill and bicycle ergometer. His results, together with those of the nine other subjects, are presented in this study.

2.3. Methods

These have been previously described on page 13.

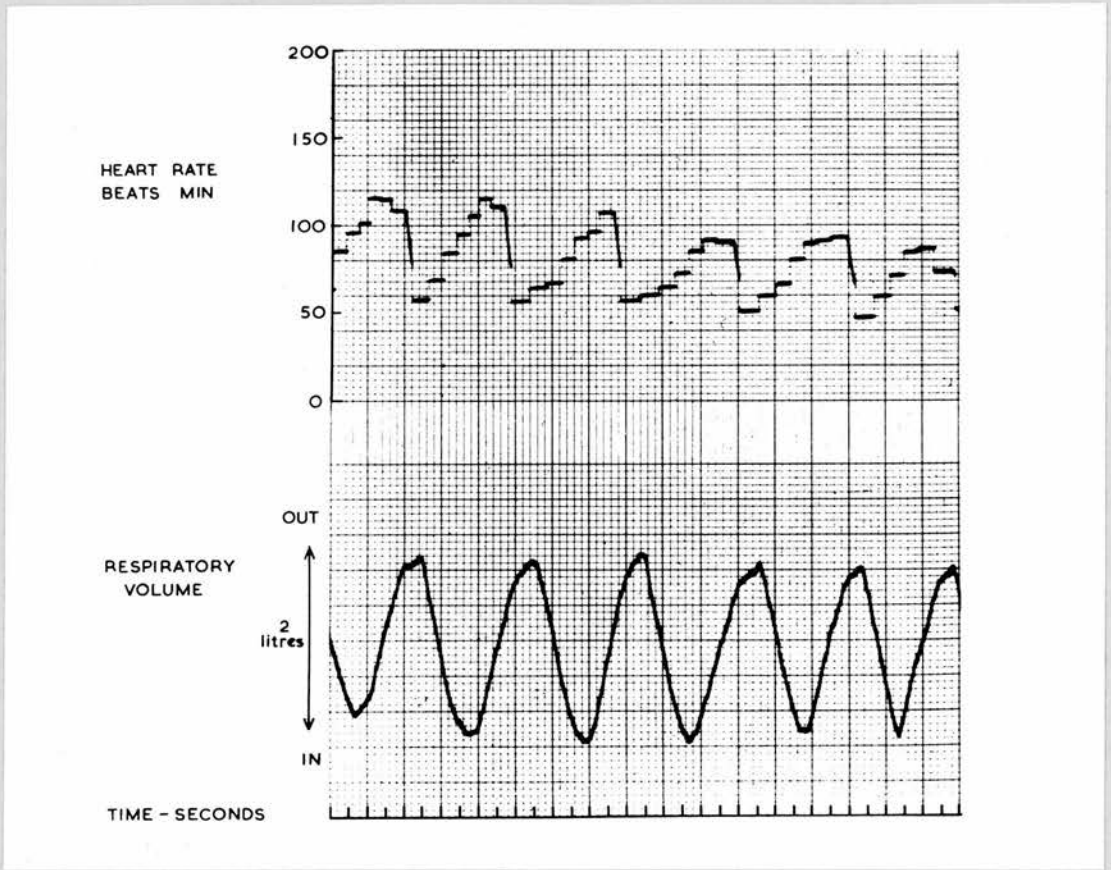


fig. 20a. A typical example of heart rate showing fluctuations. Note close association of heart rate changes with respiration; clear evidence that this phenomenon is an exaggerated form of sinus arrhythmia.

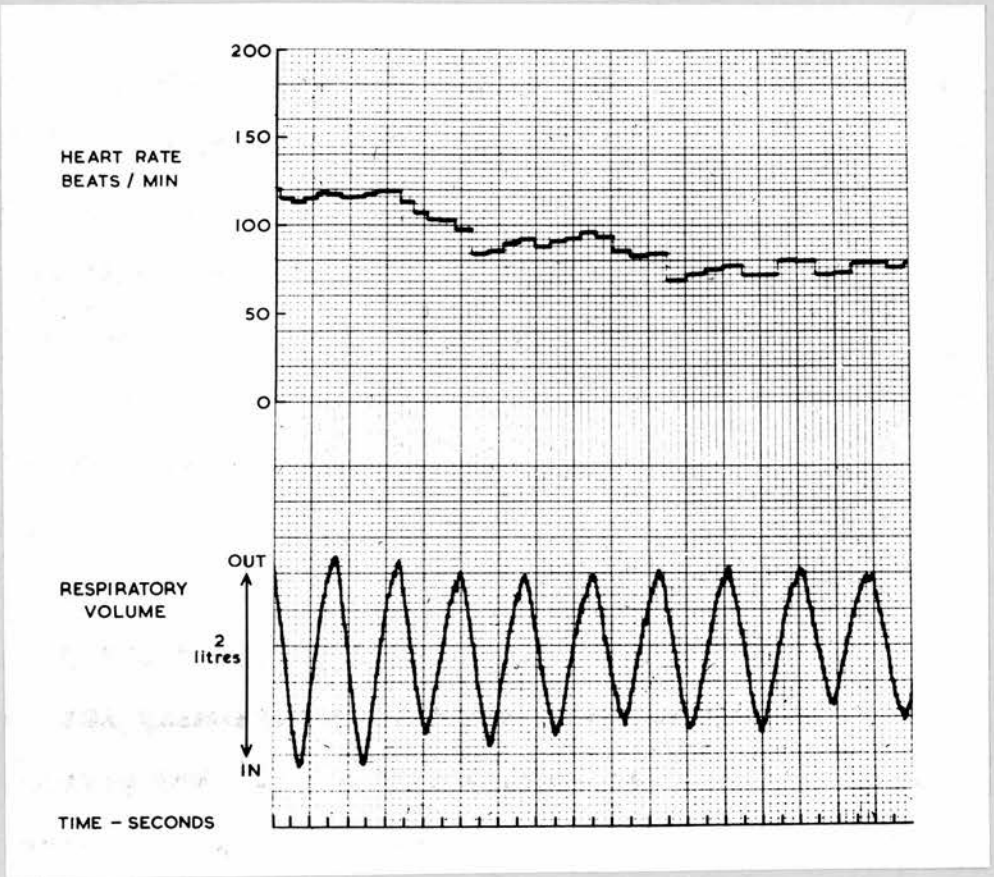


fig. 20b. A typical example of a heart rate, showing no fluctuations (group 2). The record was taken during the immediate post-exercise period.

2.4. Results

2.4.1. The relationship between respiration and the recovery heart rate

From an analysis of the individual experimental records it was found possible to divide the subjects into two groups. Group 1 contained five subjects (C.J.F., I.G.McC., K.B.S., A.M.P.B. and E.J.W.) and was characterised by a recovery heart rate pattern similar to that reported by Lamb (1961). The heart rate fell gradually for a period of 30 seconds immediately following the exercise and then showed a sudden waxing (fig. 20a). The large fluctuations in the heart rate lasted for a period of 1 - 2 minutes and then became gradually smaller as the rate and depth of respiration returned to the normal resting values observed before the commencement of exercise.

The oscillations were at all times closely associated with respiration. The heart rate typically increased within five and fell within two heart beats. The period of the waves lay between five and six seconds. The maximum amplitude observed was of the order of 70 beats/min. The accelerating phase was never more than three seconds in duration and the maximum degree of overshoot 8 beats/min. The early part of the heart rate transient was initially in phase with inspiration, but then lagged behind so that peak inspiratory volume and maximum heart rate did not coincide. The lag was never more than 0.8 seconds. During expiration the heart rate completed its climb to a maximum and then slowed suddenly and the cycle of events was repeated again at the onset of

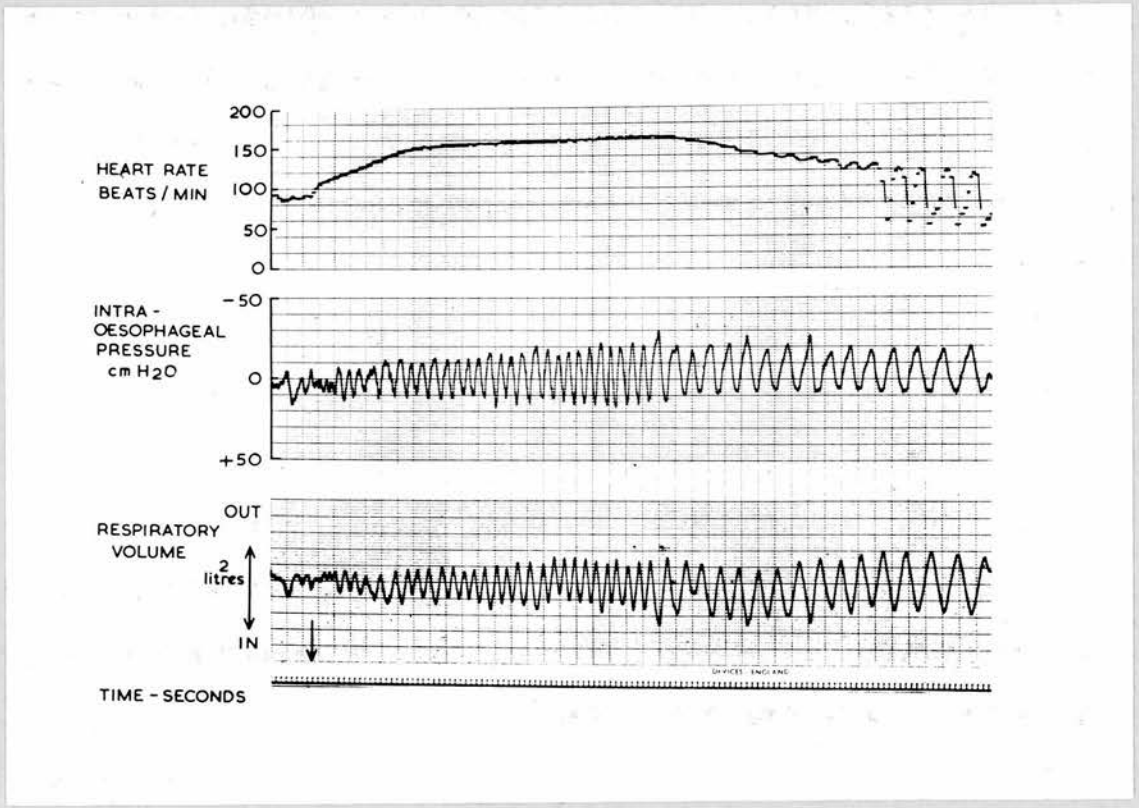


fig. 21. Relationship between (from above downwards) heart rate, intra-oesophageal pressure and respiratory volume during and following one minute of exercise. The arrow indicates the start of exercise.

the next inspiration. Maximum deceleration during the slowing phase of the heart rate was of the order of 4200 beats/min.^{2} and was always associated with a decrease in amplitude of the E.C.G. complex and in particular a marked diminution in size and length of the P wave.

The intra-oesophageal pressure was measured in one subject (fig. 21). It led inspiratory volume throughout the resting, exercise and recovery periods. During the period of oscillations this relationship was essentially maintained. No obvious abnormality in the two records was observed.

Subjects in group 2 showed no such characteristic oscillations of the heart rate (an oscillation for the purposes of this study was arbitrarily defined as a rhythmic fluctuation in the heart rate, having a mean amplitude greater than 40 beats/min.). Subjects in this group (fig. 20b) were characterised by a high exercise and recovery heart rate and more rapid respiratory rate.

2.4.2. The effect of some respiratory manoeuvres on the recovery heart rate

1. Breath-holding

During the recovery period following the second piece of exercise, subjects were asked to hold their breath after a normal inspiration during the period when the heart rate was fluctuating markedly. In some subjects this manoeuvre abolished the oscillations, in others it considerably modified them, but did not eliminate them completely (fig. 22). Following the onset of the breath-holding period the phasic

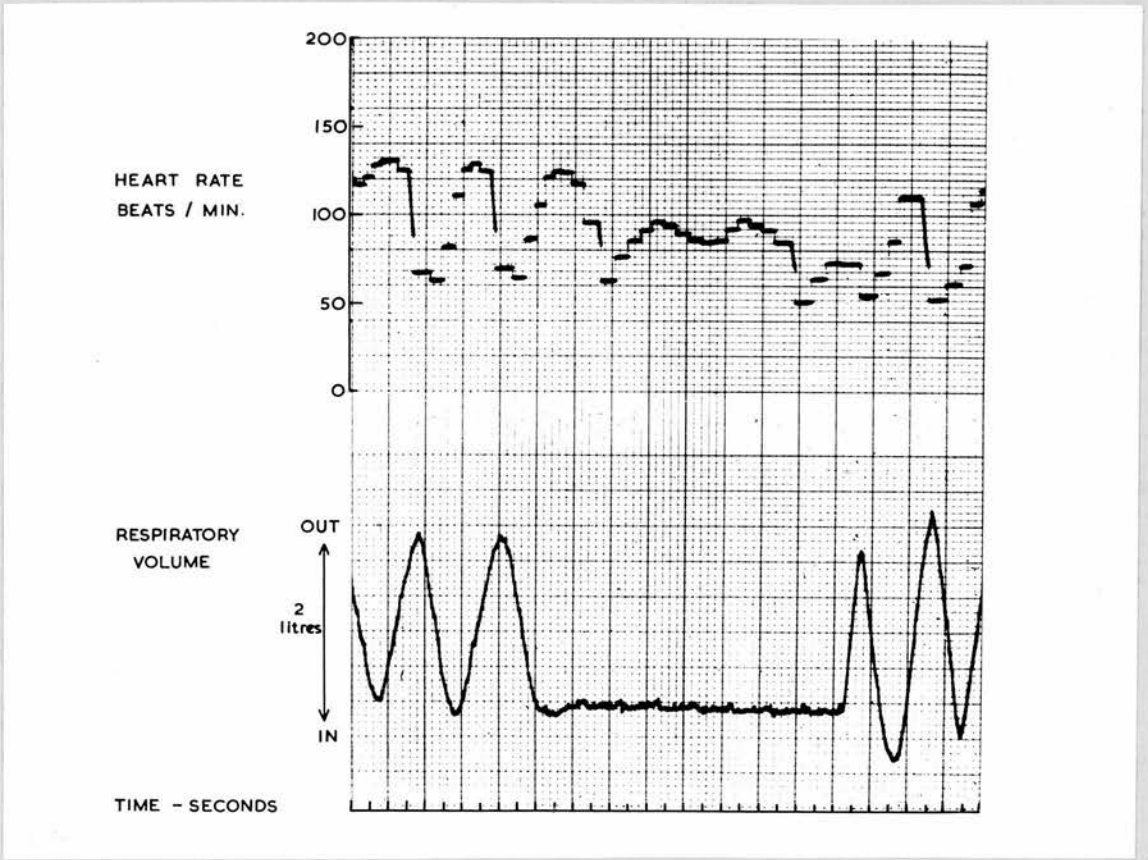


fig. 22. The effect of breath-holding on the heart rate pattern after exercise. The manoeuvre considerably modifies, but does not completely eliminate the observed fluctuations.

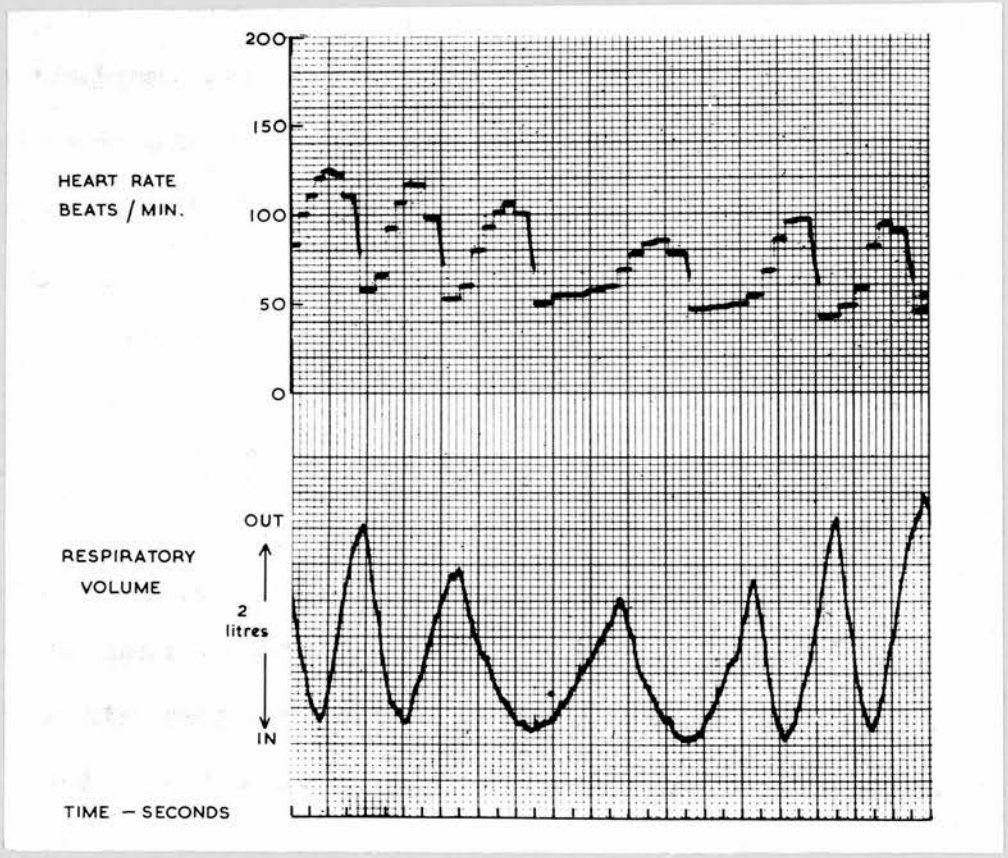


fig. 23. The effect of voluntarily altering the respiratory pattern on the heart rate. A large breath at a lower respiratory frequency produces a significant change in the pattern of the fluctuations. The basic waveforms become more clearly separated (cf. fig.17 at rest).

fluctuation in the heart rate due to the previous inspiration completed itself and then either remained constant or exhibited a series of smooth but small fluctuations. These additional changes in the heart rate were within the same frequency range as the larger oscillations. Despite the complete absence of respiration the reasons for the smaller fluctuations in the heart rate during the complete absence of respiratory movements are for the present obscure. They could arise from two sources: Either from impulses of central origin, by irradiation from the respiratory to the cardiac centres, as has been shown in animals (Heymans, 1929), or it is just conceivable that they represent oscillating components within the heart rate control system which exist independent of respiration.

Unfortunately, a thorough investigation of this problem is not possible in man, because of the serious technical difficulties involved. During the recovery stage from exercise the subject finds difficulty in holding his breath for more than a few seconds. This limits the period of observation to one, or at the most two, fluctuations in the heart rate and this provides insufficient information from which to draw accurate conclusions. In order to maintain the breath-holding position for longer periods the subject finds it necessary to close his glottis and this inevitably gives rise to an increase in pressure in the thoracic cavity and a rise in heart rate similar to that described for positive pressure exertion at rest (page 32). This effect completely masks the true response of the heart rate to breath-holding during

the recovery period when both the circulation and respiratory rate have become enhanced as a result of the previous exercise.

2. Artificially increasing or decreasing the subject's respiratory rate

The oscillations in group 1 could be abolished by asking subjects to perform manoeuvres which increased their respiratory rate. Large fluctuations in the heart rate were never observed in subjects who inhaled at a respiratory rate greater than 15 breaths/min. Decreasing the respiratory frequency of the subject during the period of oscillations resulted in the waveforms becoming more separated (fig. 23). It will be noted that a similar response was found at rest in subjects who were asked to breathe at different respiratory frequencies (see fig. 17, page 28).

2.4.3. The effect of atropine on the recovery heart rate

The intravenous injection of 1.2 mg. atropine, given thirty minutes before exercise, served to raise the resting and recovery heart rate and completely abolish the oscillations.

A similar result was obtained by chance during the experimental period through one of the subjects in group 1 contracting mumps. The period of enforced bed rest which followed the virus infection obliterated the previously-observed arrhythmic response of the heart rate. It was only following a short period of training (running daily on the treadmill) that the characteristic fluctuations began to return (fig. 25). During the convalescent period when the subject had returned to daily work and for all practical

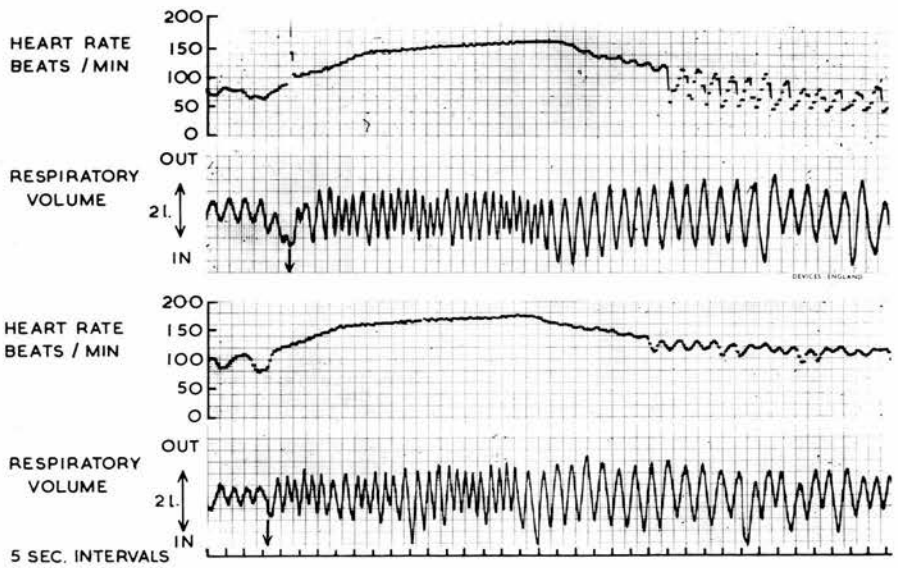


fig. 25. The effect of a period of enforced bed-rest on the exercise and recovery heart rate pattern (lower record). Following a period of training (upper record) the characteristic pattern of oscillations returned. Arrows mark the beginning of one-minute periods of exercise (11.27 km./hr. up 5%).

purposes could be assumed to be back to normal health, several attempts were made to reproduce the former recovery heart rate response. The exercise was varied, artificial respiratory and postural manoeuvres were tried, but all were without avail. The exercise and recovery heart rate remained high and was uninfluenced by the efforts of the experimenter.

2.5. Discussion

The results are in agreement with some of Lamb's findings in that the magnitude, shape and time course of the cardiac oscillations are similar in both studies and only appear in half the subjects investigated. Further, the likelihood that the effect is mediated through the vagus and therefore dependent on vagal tone is also indicated, as (1) the cardiac oscillations were not observed in subjects with relatively high exercise and recovery heart rates; (2) the effect was completely abolished by an intravenous injection of 1.2 mg. atropine; (3) following a period of enforced bed rest the fluctuations in heart rate disappeared and only reappeared following a period of training; and (4) during the slowing phase the P waves of the E.C.G. were markedly diminished in size and length, a finding consistent with a slower rate of depolarisation spreading through the atria and the release of A.Ch. (Hoffman and Suckling, 1953), but his major assertion that "the fluctuations bear no obvious relationship to respiration" has not been confirmed by this study. At all times the cardiac oscillations in this investigation were closely associated with respiratory pattern. They could be modified by manoeuvres designed to alter the respiratory pattern and abolished by a period of breath-holding, and therefore supports the early observation of Davies and Neilson (1965) that this phenomenon is an exaggerated form of sinus arrhythmia.

The effect differed only in magnitude from the response of the heart rate to a series of inspiratory transients at

rest; the period and shape of the wave form was the same in both cases. In describing the resting heart rate and respiration in Chapter 4, it was shown that the relationship between the two variables was not only frequency dependent, but probably affected, at least in part, by afferent impulses from baroreceptors situated on the left side of the heart stimulated by sudden changes of blood flow within the pulmonary circuit. It is, therefore, to be expected that following a short period of exercise when the respiratory pattern has become slower and deeper, the transient fall and rise of blood pressure within the thoracic region will become more marked and produce optimum conditions for sinus arrhythmia. This will tend to be superimposed on a high degree of vagal activity in some subjects, bringing the heart rate down to its former resting level to produce large rises and falls in heart rate for short periods of time in the immediate post-exercise period.

In subjects where these conditions are not met, increased arrhythmia is unlikely to occur. Rapid and shallow respiratory pattern will merely give rise to distortion of the inspiratory heart rate transient (cf. fig. 17) and result in waveforms of reduced amplitude dependent on the degree of vagal tone.

It is difficult to define groups 1 and 2 precisely in terms of these two factors, since vagal tone in the intact human cannot be measured, but nevertheless, the differences in heart rate recovery and respiratory rates observed between

the two groups of subjects suggest that they may be the main determinants of the degree of fluctuation observed in any one subject. It would be interesting to know the precise relationship between a given vagal tone and rhythmic increase and release of pressure in the thoracic region, and the subsequent rise and fall of blood pressure produced by a changing respiratory pattern in order that a final appraisal of the phenomenon of cardiac arrhythmia could be made.

Summary and Conclusions

At rest

The relationship between respiration and heart rate was investigated in ten subjects and it was found that:

1. The response of the heart rate to a fast inspiration was well defined. The averaged results of 97 responses showed that inspiration produced a biphasic fluctuation in the heart rate of 15.9 beats/min. mean amplitude, 13 seconds' duration and 1.5 beats/min. overshoot, representing 9.4% of the total response.
2. The response, if any, of the heart rate to a fast expiration was more variable and difficult to demonstrate. The mean of 87 step expiration responses produced a small delayed rise in heart rate of 5.5 beats/min. This could be reduced by manoeuvres designed to aid the relaxation of the muscles of the abdomen during the breath-holding period. When a step expiration followed a step inspiration, more often a fall in heart rate was observed.
3. There was no support found for the theory first put forward by Clynes that changes in heart rate with respiration are initiated by two stretch receptor mechanisms, one sensitive to inspiration and one to expiration, or that cardiac fluctuation lagged behind respiration by five seconds (Manzotti, 1958).

4. The phasic relationship between heart rate and respiration as described by Angelone and Coulter (1964) was shown to be due to the shape and form of the inspiratory transient. The constant three-second delay which occurs between the onset of inspiration and the fall in heart rate inevitably produces an increase in the phase lag between the two variables as the respiratory rate increases.

5. The underlying mechanism of sinus arrhythmia in man has been discussed and it was suggested that, though a stretch receptor might be involved, it is probable that haemodynamic factors play a major part, the rise and fall of the heart rate being affected by afferent impulses arising from the vasoreceptor on the left side of the heart as a result of blood flow changes which accompany respiratory movements.

<u>During recovery from exercise</u>

6. From the analysis of individual records it was possible to divide the ten subjects into two groups. In the first group the heart rate fell smoothly from the exercise rate of 160 beats/min. to the resting level. In the second group the heart rate decreased from the exercise level to about 125 beats/min. and then fluctuated rhythmically. The rhythmical oscillations were clearly associated with respiration and it was therefore suggested, contrary to Lamb (1963) that this phenomenon was an exaggerated form of sinus arrhythmia.

7. The mean amplitude of the heart rate waves was 60 beats/min., representing a 50% change in heart rate and the duration was 5-6 seconds. Typically, the heart rate fell from its highest to its lowest value within two heart beats and recovered more slowly within five beats. The rhythmic response of the heart rate lasted from 1-2 minutes and died away gradually as respiration returned to its normal resting level.

8. The underlying physiological mechanism responsible for these changes was discussed and at least two factors, vagal tone and respiratory rate, were identified as being important. It was suggested that the greater part of the effect was due probably to bursts of vagal activity reinforced by receptors on the output side of the heart sensitive to blood pressure.

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Part II

PHYSICAL WORKING CAPACITY IN MAN

INTRODUCTION

The assessment of a person's capacity for physical work is a normal requirement in the medical, military, industrial and athletic fields. In clinical medicine it is important to be able to make objective and quantitative measurements of a patient's physical condition, especially if he is undergoing a programme of convalescence and rehabilitation in order to make a quick and effective return to daily life. Decisions for or against compensation and surgical operation may hang in the balance and depend on valid information being available on a patient's physical working condition. It is, therefore, regrettable that the attempts made in clinical medicine to assess a patient's degree of impairment are carried out subjectively, based on the case history. This can never be truly objective, since it depends on the patient's own assertions. These are coloured by his motives and depend on the personality and intelligence of the physician.

In the Armed Forces a large amount of physical exertion is necessary, especially by ground troops in times of war. In dangerous situations a man's life may depend on his ability to exert himself physically. The War Office depends on the help and advice of the medical profession in the selection of recruits to undergo arduous training and in assessing the physical potential of normal healthy men. In the industrial field, too, the clinician's and physiologist's advice is needed to help set safe work loads and suitable rest pauses in order to avoid undue stress and fatigue during daily work.

In industries such as coal mining and forestry, men of exceptional physical condition are required and need to be screened by a doctor before employment. In sport, athletes and professional games players often require help and guidance during training and times of injury. The trained doctor is often ill-equipped to help. The underlying reasons for this may be found in current textbooks of medicine. Of ten books selected at random and published in the last five years, not one gave either any information on physical working capacity or any description of objective tests of exercise tolerance. The intending doctor is not even made aware of this important field and it is, therefore, not surprising that in later life has has to rely on his own subjective assessment of fitness and the patient's story. Textbooks of cardiology give scarcely better treatment. Of five current textbooks examined, one (Levine, 1958) did not mention the subject and three (Friedberg, 1956; Scherf and Boyd, 1948; and Evans, 1948) conclude that the clinical history is often a better guide to the patient's response to exercise than any of the utilised tests. White (1951) in his standard text book on heart disease recommends: "Climbing a flight or two of stairs at an ordinary rate of speed, climbing a hill of moderate grade at moderate pace, walking fairly rapidly on the level, or lifting and carrying a handbag, suitcase or heavy overcoat."

It would seem that the medical student in training is either given no quantitative information on the measurement of working capacity or, in the rare instant, advice of a

qualitative nature. Little or no attempt is made to define and measure physical working capacity (PWC) objectively. After nearly half a century of applied physiological research this is a regrettable state of affairs.

In the second part of this thesis an attempt is made to define working capacity in terms of oxygen utilisation and energy expenditure, and determine how far it is possible to estimate exercise capacity from respiratory and heart rate measurements simple enough to be applied routinely in both the clinical and the exercise laboratory.

CHAPTER 3

Maximum oxygen uptake

3.1. Physiological background

The main barrier to progress and a wider acceptance of the need for research in the field of working capacity has been the failure to appreciate the underlying physiological principles on which the measurement of PWC is based. Too often PWC has been confused with overall physical fitness. These two terms have been used synonymously in the literature which has given rise to an ill-defined area of investigation. Physical fitness is essentially a qualitative expression of an individual's physical condition. It describes the ability to perform a given task efficiently and without undue fatigue. In physiological terms Darling (1947) describes fitness as "..... the ability of the organism to maintain the various internal equilibria as closely as possible to the resting state during strenuous exertion and to restore promptly after exercise any equilibria which have been disturbed." The definition implies that a person with a high standard of physical fitness will perform a task more efficiently and economically than someone in poor physical condition. On the surface this would seem reasonable, but a careful consideration of the different forms of human activity soon renders this general definition untenable.

The effective performance of any piece of muscular

exercise will demand a combination, in different proportions, of skill, strength, mobility and endurance. The nature of the task will determine the different physical qualities required and the overall efficiency by which it is performed will depend on how far the individual is able to meet the demands on his body by virtue of his natural endowment and degree of training. Fitness for many forms of physical activity will demand little in the way of strength and endurance; interest will be partly centred around a highly skilled and artistically-satisfying performance. The efficiency and inefficiency of the exercise will be judged in these terms and physiological cost will be of little or no importance. Clearly, if we accept this view, fitness can only be defined in relation to a specific activity. Any attempt to consider fitness for all forms of human endeavour quickly leads to vague generalisation and ultimately a violation of the truth.

The definition and measurement of working capacity must be set against this background. It is concerned with a specific type of fitness, namely, the capacity of the individual to undergo prolonged physical exertion. From a strictly physiological viewpoint this will depend on the person's ability to utilise oxygen and expend energy. The ultimate measure of a person's exercise capacity will be the maximum amount of oxygen he can transport and utilise in unit time. This is the ultimate measure of the combined circulatory and respiratory systems. It characterises the upper limit of performance in a remarkably consistent way.

At rest a fully trained Olympic athlete will inhale some 5-8 litres of air per minute, from which about 250 cc. of oxygen is extracted and used by the body. During maximal exercise these figures may well rise to 150 litres and 5000 cc. respectively which represents a twenty-fold increase of his basal rate. As soon as the oxygen supply fails to meet the demands of the active muscles, fatigue products quickly accumulate and exercise must stop. The maximum oxygen uptake (Max $\dot{V}O_2$) of an individual is, therefore, a true reflection of the factors which govern the transport of oxygen from the outside air to its site of energy utilization in the body. It is the only defensible "a priori" criterion of a man's fitness for physical work: It defines the actual amount of work he can do. The method used by Taylor et al. (1955) for the direct determination of Max $\dot{V}O_2$ has been shown to be independent of skill factors and to have a coefficient of reliability of 0.95. Undoubtedly if it could be used with all groups of subjects it would be an extremely useful physiological tool. Unfortunately, its direct determination involves a series of laborious and, for the subject with impaired working capacity, uncomfortable experiments. To obtain maximum values, repeated work periods of at least three minutes are required over a period of 2-3 experimental days. The risk of over-strain with older subjects and patients makes the procedure inappropriate and inadvisable. At least one patient has died on the treadmill during maximal effort (Bruce et al., 1951). Further, subjects who are not interested or do not partake regularly in physical exercise

do not enjoy being run to exhaustion and it is very difficult for the observer to be sure of their complete co-operation. In order to encourage a wider application of the concept of Max $\dot{V}O_2$ while avoiding the drawbacks of procedures involving maximal exertion there is a great need in the medical and physiological fields for a simple safe test which would allow the prediction of a person's maximum capabilities from data collected at submaximal loads.

The nature of the problem is complex, but one possibly simple solution has been offered by Åstrand and Rhyming (1954). They have suggested that the rectilinear relationship between heart rate and O_2 uptake which has been established many times over a wide range of values (Benedict and Cathcart, 1913; Bock et al., 1928; Robinson, 1938; Taylor, 1941; and Berggren and Christensen, 1950) might be used to predict the Max $\dot{V}O_2$ of an individual directly. They have presented a nomogram based on data taken from a large number of healthy 18-30 year-old subjects from which they claim Max $\dot{V}O_2$ can be determined (as twice the O_2-uptake corresponding to a heart rate of 128 in males and 138 in females) with an accuracy of $\pm$ 10% provided heart rates below 125 beats/min. are not used.

This general conclusion has been supported more recently by the work of Wyndham and Ward (1957) and Asmussen and Molbech (1959), though both authors have suggested modifications to the original Åstrand-Rhyming technique. The former used as their basis observations of Berggren and Christensen (1950) and Åstrand (1952) that Max $\dot{V}O_2$ correlated with a heart

rate value of 194 ± 1.6 beats and from their observations on three groups of people, cardiac patients, sedentary laboratory workers and well-trained Africans, suggested that Max $\dot{V}O_2$ could be derived from measurements of heart rate and O_2 uptake taken at three different levels of work by extrapolation to a fixed value of 190 beats/min. Asmussen and Molbech, on the other hand, have suggested the use of the formula derived by Asmussen and Hemmingsen (1958) from the original data of Robinson (1938) and Åstrand (1956) to predict Max $\dot{V}O_2$.

In deriving the formula it was assumed that if maximum O_2 uptake and heart rate were reached at the same level of work, then

$$\frac{\Delta P}{\Delta O_2} = \frac{\Delta P \text{ Max}}{\Delta O_2 \text{ Max}} \quad \ldots\ldots\ldots (1)$$

Where ΔP is the increase in pulse rate during the work period, ΔO_2 is the increase in O_2 uptake during the work period.

ΔP Max is the maximum increase in pulse rate during the work.

ΔO_2 Max is the corresponding increase in O_2 uptake.

From equation (1) it follows that

$$\Delta O_2 \text{ Max} = \frac{\Delta P \text{ Max} \times \Delta O_2}{\Delta P}$$

and therefore the theoretical Max $\dot{V}O_2$ is

$$\text{Max } \dot{V}O_2 = \Delta O_2 \text{ Max} - O_2 \text{ rest}$$

Asmussen and Molbech claim, together with the original

authors, that the formula could be used with patients and normal subjects between twenty and sixty years of age.

The use of the heart rate to predict the actual Max $\dot{V}O_2$ of an individual differs in principle from other tests so far proposed, based on either the recovery heart rate (e.g., Havard fatigue, Johnson et al., 1942 and Masters two-step test, Masters and Oppenheimer, 1929; and Masters, 1935), or the exercise rate (e.g., Wahlund test, Wahlund, 1948; and Balke test, Balke, 1952) and suggests a more rational approach to the measurement of working capacity. The procedure is safe, easily administered, and with recent advances made in cardiotachometry, suitable for routine use and for these reasons would seem worthy of further study.

Unfortunately, serious doubts surround the use of the exercise heart rate as a criterion, especially at lighter work loads. It is known, for instance, that the heart rate can undergo random day-to-day variation quite independently of O_2 uptake during light to moderate exercise. It is affected by temperature (Christensen, 1932), dehydration (Saltin, 1964) and training (Knehr, et al., 1942). All these factors could give rise to serious error when single pulse counts are used, as in the Åstrand-Rhyming and Asmussen-Molbeck tests, and impair the accuracy of the procedure in the individual case. Further, the validity of all procedures which use submaximal heart rate and O_2-uptake data to assess the Max $\dot{V}O_2$ of the individual depend upon the assumption that 1) the relationship between the two variables is linear up to and including maximum levels of work, and 2) the

variability of an individual's maximum heart rate round the population mean for a particular age group must be so small as to introduce negligible error.

Preliminary work from this laboratory had indicated that neither of these assumptions was entirely correct, even in normal healthy subjects. The maximum heart rate was found to be higher in sedentary subjects as compared with more athletic, and O_2-uptake reached maximum values more slowly than heart rate, giving rise to serious non-linearity in the heart rate - O_2-uptake line as near maximal effort was reached. Thus, if extrapolation from submaximal values of heart rate and O_2-uptake to a fixed maximal pulse had been used to assess Max $\dot{V}O_2$ this would have resulted in a gross under-estimation of an individual's ability to perform at maximum effort.

In this study an analysis of the heart rate - O_2-uptake curves of ten subjects is presented. Some attempt has been made to assess 1) the overall limitation of the different methods for predicting Max $\dot{V}O_2$ from heart rate and $\dot{V}O_2$ data collected from submaximal levels of work; 2) the magnitude of the error due to: a) random variations in the measurement of heart and $\dot{V}O_2$ under normal standard laboratory conditions, b) non-linearity in heart rate - O_2-uptake time, and c) the inability of all subjects under consideration to reach approximately the same maximum pulse; and 3) the feasibility of substituting predicted measurements of $\dot{V}O_2$ from a mean population graph relating O_2-uptake to work rate for actual values of $\dot{V}O_2$ in a scheme for measuring Max $\dot{V}O_2$ under field conditions.

Originally, it was hoped to include a wide age range of experimental subjects, and although these were available in Edinburgh, it was felt unwise to risk exercising elderly people, since adequate medical supervision could not be provided. In the circumstances prevailing this was an unavoidable decision, but it has tended to limit this part of my work to a study on young healthy adults.

TABLE III

Physical characteristics of the ten experimental subjects.

Subject	Age (years)	Weight (kg.)	Height (cm.)
R.M.M.	19	63.85	168.13
J.T.H.	20	89.00	182.50
D.S.O.	21	71.09	180.62
F.E.G.	20	62.99	170.00
W.J.S.	23	75.40	181.25
R.W.L.	23	61.10	165.00
I.R.F.	23	83.30	183.13
C.F.J.R.	25	77.37	175.63
A.F.M.	21	66.25	177.50
A.E.C.C.	19	67.95	173.75

3.2. Procedure

Ten healthy male subjects were studied. All were unpaid volunteers and apart from the athletes, were selected at random from the main body of the Edinburgh University student population. Details of their age, weight and height are given in table III. The experiments were carried out on two separate days. Each subject was also required to attend an additional preliminary session to become accustomed to the respiratory apparatus and the motion of the treadmill.

Day 1

Subjects were studied after a light lunch or breakfast. They refrained from drinking coffee or smoking eight hours prior to the test. During the preliminary period a warm-up (4 m.p.h. on the level) was given, the bladder emptied, height and weight taken, and electrodes fixed in position. The subject then rested quietly in a comfortable chair placed on the treadmill for forty minutes, during the last ten of which heart rate, respiratory frequency and oxygen uptake were measured. One minute before the commencement of exercise, the order was given to start and the chair was removed. The last few seconds were counted aloud until zero time, at which the treadmill was started and the subject exercised up a 1% gradient for six minutes. $\dot{V}O_2$ was measured during the fifth and sixth minute of exercise. During the recovery period, which lasted for twenty minutes, or until the heart rate exceeded the resting rate by no more than 5 beats/min., the chair was replaced. The next exercise which was set by increasing the gradient, followed at once, using exactly the

same procedure as before. During the course of the day six exercise intensities were usually performed: 1%, 3%, 5%, 7%, 9% and 12%, though some subjects were asked to perform additional pieces of work at 0%, 15% and 18% (see table XX).

The subjects exercised in vest, shorts and plimsolls. After every second piece of exercise the respiratory tubing and valves were washed out and the subject was free to empty his bladder if he wished. The break between the last two grades of work was extended to thirty and sixty minutes respectively, to allow the subject to return to near resting conditions. Through the exercise and recovery periods electric fans were directed at the subject and the temperature of the treadmill room was kept approximately constant at 68°F.

Day 2

The maximum oxygen uptake was determined using a method similar to that described by Taylor et al. (1955). A ten-minute warm-up period (4 m.p.h. at 10% gradient) was followed by a fifteen-minute rest period. The first test run was then carried out, usually at 7 m.p.h., 2.5% gradient for the normal subject and 7.5% for the athletes. Before the treadmill was started the subject was connected to a Douglas bag by a "Bannister" valve and smooth bore tubing, and during the first 1¾ minutes of the run, expired air was allowed to wash out the dead space of the system. Expired air for analysis was collected during the succeeding one-minute period and later analysed for O_2 and CO_2 content by the Haldane method. Heart rate was measured continuously during the exercise period. After a fifteen-minute rest period the work load

was increased by raising the gradient 2.5%, the speed remaining constant and the whole procedure repeated. Increments of 2.5% were used until the subject was exhausted.

Criteria for maximal values

Hill et al. (1924) have shown that there is a linear relationship between $\dot{V}O_2$ and work load until the Max $\dot{V}O_2$ is reached. Work rates beyond this point merely result in a flattening of the curve and an increase in oxygen debt. Fatigue quickly sets in and the subject has to stop exercising. Usually, the point at which the $\dot{V}O_2$ curve ceases to rise is taken as the Max $\dot{V}O_2$. In well-motivated subjects this point is not very difficult to ascertain, but in others who are not used to, and do not enjoy being run to complete exhaustion, it is not possible to judge whether they have made an all-out effort. It is necessary, therefore, to apply independent criteria and obtain proof in order to guarantee that the data obtained is truly representative of maximal achievement.

The method of Wyndham et al. (1959) is commendable in as much that it avoids the use of arbitrary fixed values of lactate (Åstrand, P.O., 1952; Åstrand, P.O. and Saltin, 1961; Astrand, I., 1960) and pulse rate to characterise maximal load on the subject. The best fitting curve is drawn through a large number of $\dot{V}O_2$ points obtained from several submaximal and maximal work loads performed on different occasions. The theoretical asymptotic value of Max $\dot{V}O_2$ is calculated and later compared with the actual level of work reached. Unfortunately, to be of value, this method demands a great number of separate $\dot{V}O_2$ determinations which seriously reduces its usefulness for

routine application.

Both Mitchell et al. (1958) and Taylor et al. (1955) have shown that by raising the grade, using 2.5% measurements and keeping the speed constant at 11.27 km./hr., the $\dot{V}O_2$ increases uniformly. In the former case, plots of $\dot{V}O_2$ against workload showed that until a maximal value was attained, $\dot{V}O_2$ rose by 299.3 cc./min. (SD - 86.5 cc./min.) With each increase of workload thereafter, $\dot{V}O_2$ either remained steady or began to decline. By ensuring that two consecutive determinations of $\dot{V}O_2$ at maximal level did not disagree by more than 150 cc./min. or 2.1 cc. kg., proof of maximal exertion could be readily ascertained. A similar procedure has been adopted in this study. The expired air was analysed and $\dot{V}O_2$ calculated for each subject; when two consecutive values at the highest loads differed by more than 150 cc./min. it was concluded that maximal effort had not been achieved and the subject was required to attend the laboratory again until two grades of work were found which met with this criterion.

3.3. Methods

In all experiments which involve the collection and analysis of respiratory gases there is always a risk of error arising through either faulty technique or storage of the gas sample. A related problem is that of resistance to air flow when conventional rubber tubing and mouth pieces are used in experiments involving high flow rates. As it was known beforehand that this study would involve ventilation rates in excess of 120 litres/min. and a possible delay of several hours between actual collection and analysis of the gas samples it was felt necessary to carry out a systematic investigation of the whole problem of expired air collection, storage and analysis techniques. This has been presented as an appendix to this thesis.

Expired air volume

A low resistance dry gas meter (Parkinson Cowan Ltd.) was used in a manner previously described (Appendix 1, page 9). Inspiratory volume was continuously monitored via a relay switch on the meter and expired air was collected into Douglas bags. The meter was calibrated at frequent intervals by exercising a subject into a steady state at several different work rates on the treadmill and then measuring the ventilatory volume with the meter and Douglas bag simultaneously, correction being made for temperature and the difference in N_2 content of inspired and expired air.

A "Bannister" type mouthpiece in combination with $1^1/8$" smooth bore rubber tubing (Dunlop Rubber Co. Ltd.) was used to connect the subject to the meter and Douglas bag. The

dead space of the valve was measured by filling with water and estimated to be approximately 40 cc. This particular combination of mouthpiece, respiratory tubing and meter was found by experiment to produce the least resistance to air flow during high ventilation rates.

Expired air analysis

The Beckman E_2 analyser was used for the analysis of oxygen in the expired air samples. Gas was transferred direct from the Douglas bags into oiled syringes and conventional glass tonometer tubes. By taking this double precaution, frequent calibrations and "spot" checks on the method could be carried out. Further details of the accuracy and reliability of the method are given in Appendix 1 on page 15. The CO_2 content of the expired air samples was analysed, using the Lloyd-Haldane apparatus. Duplicate analyses were required to agree within 0.05 vol. %.

Heart rate

The method used for the continuous monitoring of heart rate has been described on page 13. The output of ratemeter, together with the respiratory frequency and volume signals were displayed on a four-channel pen recorder.

Correction of data

In order to make valid comparisons of metabolic rate between individuals of different stature it is necessary to introduce some standard of reference. By far the most popular standard in medical literature is body surface area. The rationale for surface area correction of resting metabolic rate and cardiac output dates back to the authority of two

men, Rubner (1883) and Grollman (1932). Its use as a standard of reference for basal energy expenditure implies that metabolism is determined by the necessity to control heat loss. In physical systems the rate of cooling is dependent upon the area of the body and upon the difference in temperature between the body and surrounding atmosphere, i.e., the fall is exponential. Clearly this does not apply to warm-blooded animals. Many workers (e.g., Kleiber, 1961; and Keys and Brozek, 1953) believe that the relationship of heat production and body surface area is wholly fortuitous and ought to be discarded as a standard for metabolic data on humans.

Gross body weight has often been recommended for use as standard and is still used by the F.A.O. Durnin (1959) has shown in 130 women and 170 men engaged in a variety of occupations, that the correlation between energy expenditure and body weight is quite low ($r = 0.40$). This is not surprising when we consider that weight includes such tissues as fat and bone which are not very active metabolically. This difficulty on the surface can be overcome by correcting to "lean body mass". This can be undertaken in the laboratory with a minimum of apparatus by use of the under-water weighing technique (Brožek, Henschel and Keys, 1949), the fundamental premise being that lean mass of different individuals has a constant density. Tanner (1951), however, has shown that there is low correlation between fat, bone and muscle in the same individual, and Durnin (1965) completely rejects the idea that fat can be considered inert during

exercise involving the utilisation of oxygen.

In this study, to avoid the drawbacks arising when using surface area, gross body weight and lean body mass, a simple correction for body weight has been made and all $\dot{V}O_2$ values have been expressed in terms of a standard 65 kg. (reference) man. ~~The full~~ Some anthropometric details of the subjects ~~is~~ are given in table III. In the final analysis, it would seem to have more in its favour than any other standard of reference that can be applied routinely. Certainly during treadmill walking, energy expenditure has been shown to correlate more precisely than other variables (Mahadeva et al., 1953). The main source of error in comparing different individuals will be found in obesity. Overweight subjects may have a large lean body mass and/relatively fat free, if they are very active (Welham and Behnke, 1942). In sedentary subjects the reverse might be true. In this study the latter will be over-corrected by use of the body weight standard and be judged to be more unfit than he really is, if submaximal (heart rate) criteria are used, compared with his more athletic compatriot. The subject of obesity is obviously complex and to avoid unnecessary confusion and error, only subjects weighing between 55 and 80 kg. have been included in this study.

All ventilatory data has been expressed at body temperature, ambient pressure and saturated with water vapour (B.T.P.S.) and $\dot{V}O_2$ at standard temperature, pressure and dry (S.T.P.D.).

TABLE IV.

Submaximal values of heart rate and oxygen-uptake.

Speed km./hr.	gradient %	number of observations	$\dot{V}O_2^{65}$ cc./min. S.T.P.D.			E.H.R. - beats/min.		
			range	mean	S.D.	range	mean	S.D.
6.44	1	10	1.14-1.35	1.24	0.06	88-136	109.6	16.3
"	3	10	1.33-1.52	1.43	0.06	93-146	116.0	16.5
"	5	10	1.53-1.70	1.62	0.06	97-159	124.3	21.9
"	7	10	1.77-2.01	1.86	0.08	104-178	136.3	23.8
"	9	10	1.94-2.25	2.10	0.11	117-183	148.8	23.3
"	12	10	2.38-2.66	2.49	0.11	125-196	164.4	24.9

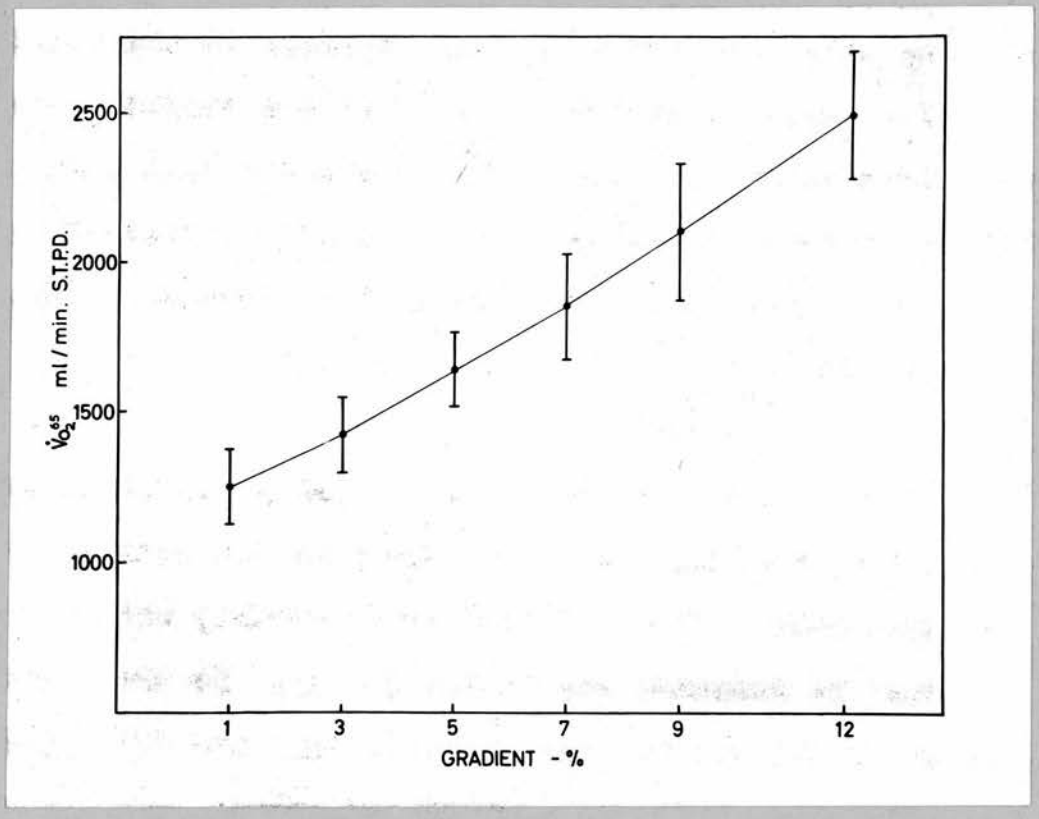


fig. 26. Oxygen uptake ($\dot{V}O_2^{65}$ S.T.P.D.) in relation to gradient at 6.44 km./hr. for all subjects
I○I mean value ± 2 x SD.

3.4. Results

3.4.1. Submaximal and maximal values of $\dot{V}O_2^{65}$ and EHR

The submaximal mean values of EHR and $\dot{V}O_2^{65}$ are given in table IV. The former is plotted against gradient in fig. 26. The approximately rectilinear relationship between the two variables serves only to confirm what has been already well documented by other workers in the field.

The small variation in $\dot{V}O_2^{65}$ at the various levels of work (coeff. of variation <10%) indicates that there was little difference between the mechanical efficiency of the individual members of the group. The regression equation relating $\dot{V}O_2^{65}$ to gradient is given by:

$$y = 0.114x + 1.08,$$

where y is the oxygen uptake in cc./min. (S.T.P.D. and corrected to 65 kg.) and x is the gradient (tan Angle) in %. The mean values of $\dot{V}O_2^{65}$ compare favourably with the ones reported by Passmore and Durnin (1955). In their extensive review of the subject they gave an equation for the relationship between energy expenditure and speed: $e = 0.8v. + 0.5$, where e = energy expenditure in kals./min. and v = speed in km./hr. According to that formula, energy expenditure whilst walking on the level for the present material should be about 1.10 L./min. which compares favourably with the observed value found in this investigation.

The corresponding EHR values show considerably greater variation at any given work load. This is due in part to the inclusion of three extremely fit athletes in the original group. Their heart rate was much lower than the group mean

TABLE V.

Maximal values of oxygen uptake, ventilation and heart rate.

	number of observations	range	mean	S.D.
Max $\dot{V}O_2$ S.T.P.D. - Litres	10	2.92-5.43	3.82	0.83
Max $\dot{V}_E$ - Litres B.T.P.S.	10	88.6-140.9	119.52	14.02
Max HR - beats/min.	10	200-182	190.0	5.6

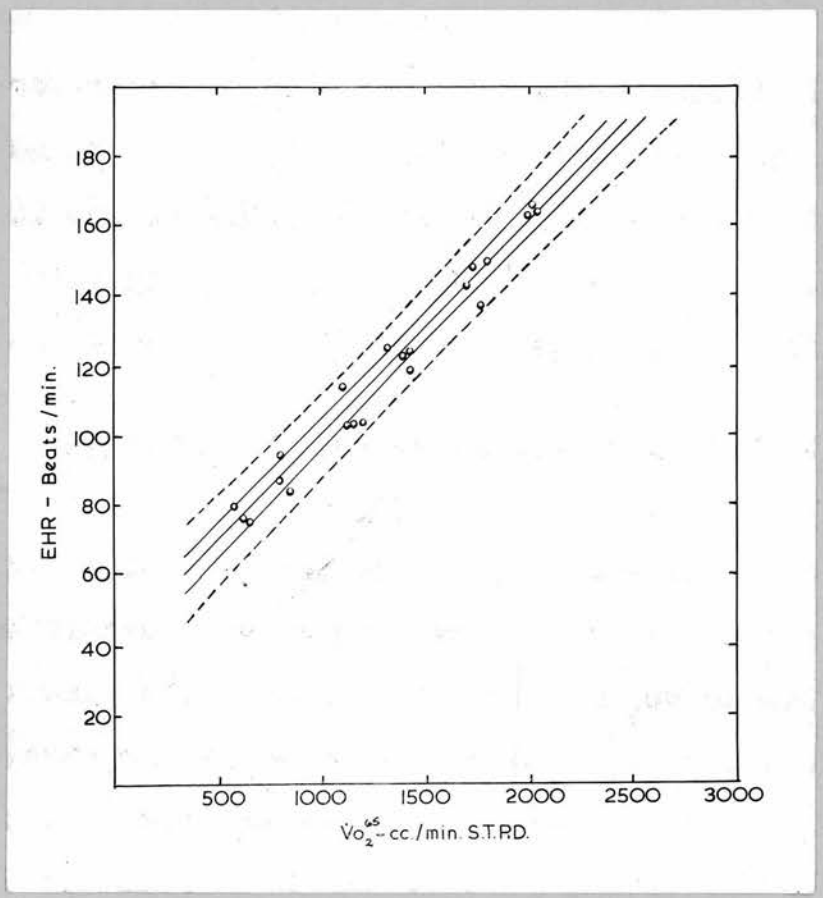


fig. 27. Regression of exercise heart rate (EHR) on O_2-uptake ($\dot{V}O_2^{65}$ S.T.P.D.). ___ 95% confidence limits for the line and --- 95% confidence limits for a new observation.

at all levels of exercise, becoming particularly noticeable at the higher rates of work (table IV).

The maximal values for $\dot{V}O_2$ [65], $\dot{V}_E$ and EHR are summarised in table V. The mean value for Max HR was 190 ± beats/min. which compares favourably with the figures of 195 (Dill and Brouha, 1937), 189 (Robinson, 1938), 194 (Åstrand, P.O., 1952) and 187 (Åstrand, I., 1960), given by other workers in the field using similar groups of subjects. The mean values for Max $\dot{V}O_2$ and Max $\dot{V}_E$ were 3.80 Litres/min. and 119.52 ± 4.43 L/min., the highest recorded values being 5.43 Litres/min. (S.T.P.D.) and 140.9 Litres/min. (B.T.P.S.) respectively.

3.4.2. The relationship between EHR and $\dot{V}O_2$

3.4.2.1. At submaximal work loads

At submaximal work loads in order to 1) test the premise that the EHR is to a close degree of approximation a linear function of $\dot{V}O_2$ at submaximal work loads, and 2) assess the possible contribution of random error and physiological variability interfering with the accurate estimation of predicted Max $\dot{V}O_2$, a large number of measurements of EHR and $\dot{V}O_2$ were made on one sedentary subject over a period of ten weeks. These points, together with the regression line of the form $y = bx + a$ where $y = \dot{V}O_2$ and x = EHR, and 95% confidence limits for the line and any new observations have been plotted in fig. 27. The line was tested for goodness of fit by means of analysis of variance. The probability of the given value of "F" being exceeded if the hypothesis of linearity under test was true, was not significant

TABLE VI.

The relationship between EHR and $\dot{V}O_2^{65}$. The individual regression equations for ten subjects of the form $y = bx + a$, where y = EHR and $x = \dot{V}O_2^{65}$.

subject	regression equation	correlation coefficient
R.M.M.	$y = 0.50x + 46.9$	.997
J.T.H.	$y = 0.52x + 49.9$	.994
D.S.O.	$y = 0.35x + 57.8$	.972
F.E.G.	$y = 0.33x + 44.0$	.994
W.J.S.	$y = 0.49x + 48.5$	.994
R.W.L.	$y = 0.55x + 63.7$	.971
I.R.F.	$y = 0.48x + 63.5$	.990
C.F.J.R.	$y = 0.46x + 38.2$	.991
A.F.M.	$y = 0.31x + 54.1$	.989
A.E.C.C.	$y = 0.50x + 56.1$	.978

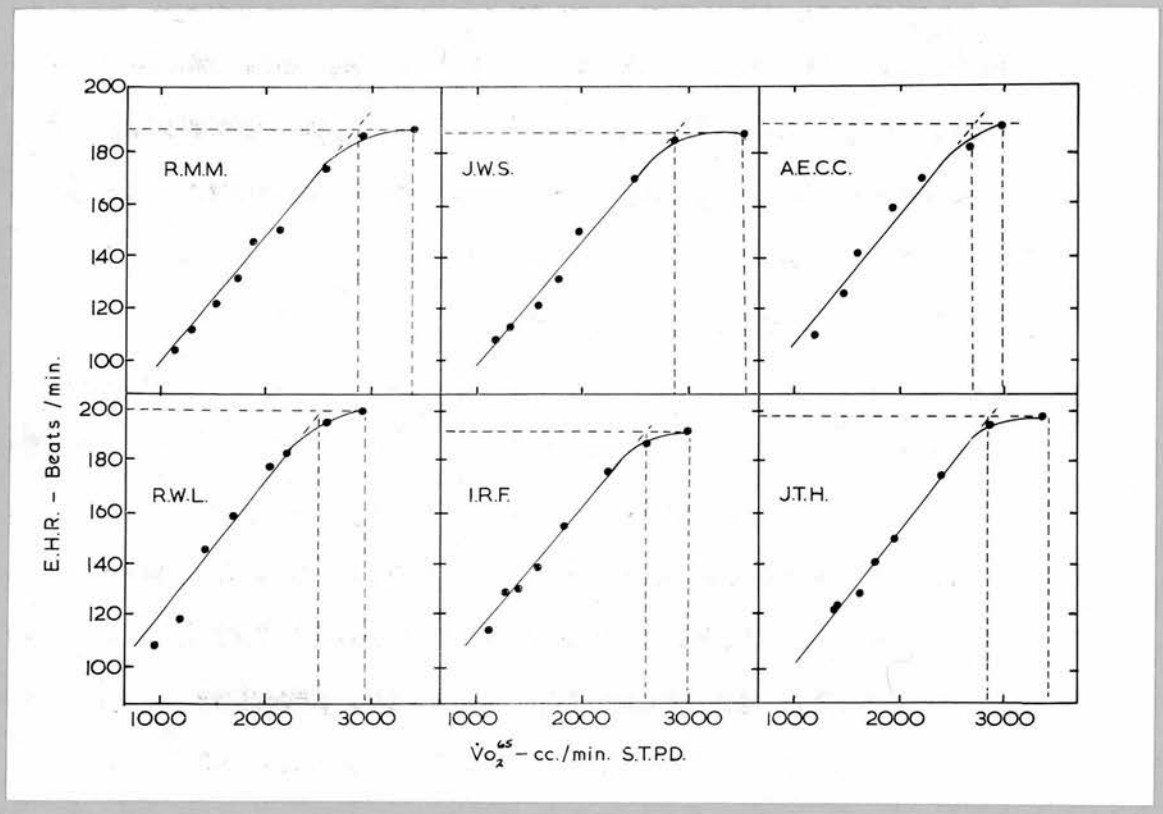


fig. 28. Exercise heart rate (EHR) in relation to oxygen-uptake ($\dot{V}O_2^{65}$ S.T.P.D.) at various work rates up to and including maximum exercise for six subjects.

($p > 0.50$) and indicated that indeed the relationship of EHR to $\dot{V}O_2$ at submaximal work loads is linear and the normal procedure of fitting a line to such data is justified.

The contribution of random error due either to natural day-to-day physiological variation or error of measurement can be assessed from the 95% confidence limits for any new observation. It is of the order of $\pm$ 207 cc. which will constitute a 7% day-to-day error in the determination of Max $\dot{V}O_2$, assuming that the EHR/$\dot{V}O_2$ line is extrapolated to a pulse rate of 190 beats/min.

3.4.2.2. <u>At maximal work loads</u>

Single measurements of EHR and $\dot{V}O_2$ and EHR were taken on ten subjects at several rates of work. The regression equation for these subjects relating EHR and $\dot{V}O_2$ are given in table VI. The correlation coefficients are in accord with those given by Erikson et al. (1946) and Taylor (1941) and lie between 0.971 and 0.997. In order to study the premise previously outlined, viz. that EHR is a linear function of $\dot{V}O_2$, up to and including maximal levels of work, the work loads of six of the ten subjects were arranged so as to form an approximate continuous gradation from the lightest to the most severe; the terminal point being the subject's Max $\dot{V}O_2$. The EHR data for these subjects has been plotted against $\dot{V}O_2$ in fig. 28. The graphs show that though a straight line relationship does exist between the two variables over the greater part of their range as near maximal levels are approached, it begins to break down and a distinct departure from linearity appears; the curve approaching a horizontal asymptotic ~~is~~ 15 EHR ~~as~~ 16 plotted

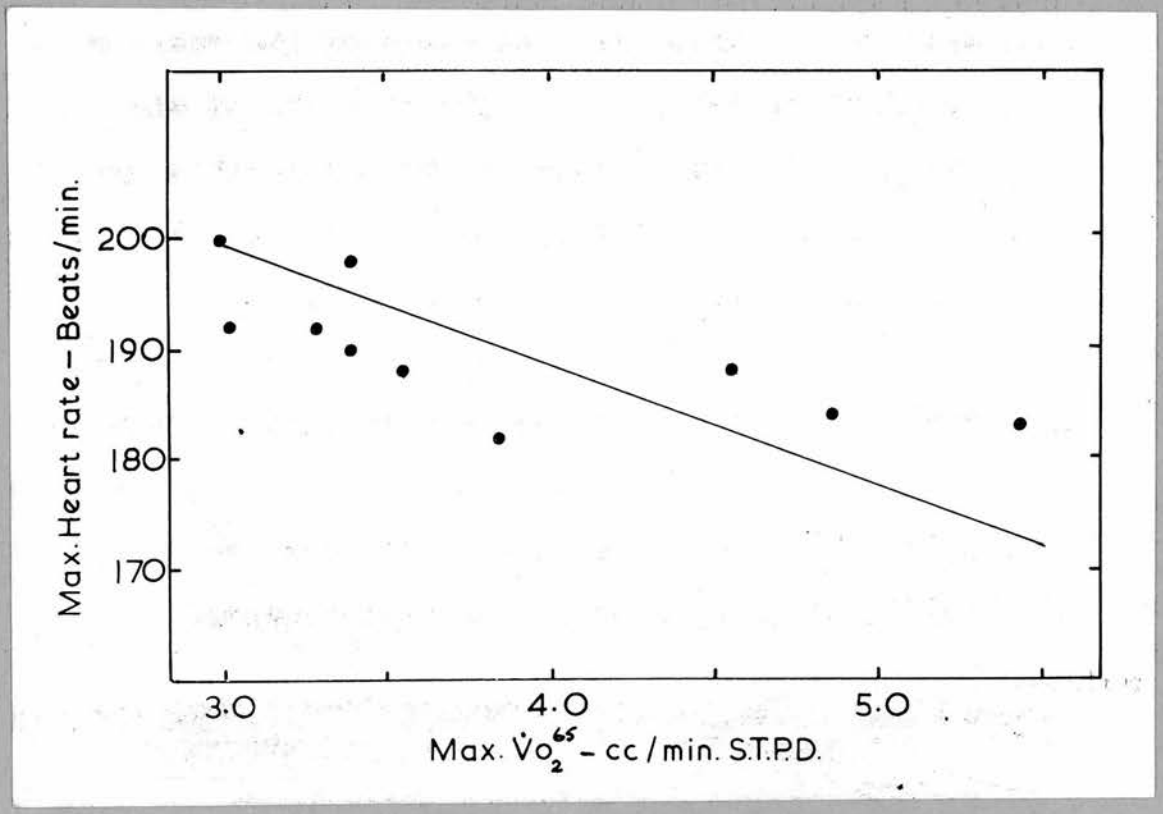


fig. 29. Maximum heart rate (Max HR) in relation to maximum oxygen uptake (Max $\dot{V}O_2^{65}$ S.T.P.D.)

on the ordinate. This means that when the EHR/$\dot{V}O_2$ line is extrapolated to a maximal value of the heart rate, the $\dot{V}O_2$ value will always be less than the observed or "true" value at the asymptotic. The magnitude of the under-estimation of the "true" value of $\dot{V}O_2$ can be seen from the figure where the straight line relating EHR and $\dot{V}O_2$ has been extended to intersect the maximum observed value of the heart rate. The bias is of the order of 652 $\pm$ 365 cc./min. at the 95% confidence level and this, compared to the error which is likely to occur from random variation (fig. 27) is significant ($p < 0.01$) and constitutes a serious limitation to all methods which aim to predict the Max $\dot{V}O_2$ from data collected at submaximal levels. All forms of extrapolation to an observed or predicted maximum pulse will lead to a bias in the estimation of Max $\dot{V}O_2$ towards a value lower than that expected from the true value, if that had been measured.

3.4.3. Individual values of maximal heart rate compared with the population mean for the ten subjects

In fig. 29 the individual maximum heart rates have been plotted against Max $\dot{V}O_2$. It will be noted that there is a slight tendency for Max HR to decrease with increasing fitness (as judged by the Max $\dot{V}O_2$). The highest rate, 200 beats/min., was recorded on the subject with the lowest Max $\dot{V}O_2$, whereas the two athletes F.E.G. and A.F.M., who ran to exhaustion on several different occasions, were quite unable to reach a heart rate beyond 182 and 184 beats/min.

TABLE VII.

Relationship of observed Max $\dot{V}O_2$ to predicted Max $\dot{V}O_2$ obtained from (1) the extrapolation of the EHR/$\dot{V}O_2$ line to 190 beats/min.; (2) Astrand-Rhyming nomogram using a single measurement of EHR and $\dot{V}O_2$; and (3) Asmussen-Molbech formula.

Subject	Observed Max $\dot{V}O_2$ (Litres/min.)	Predicted Max $\dot{V}O_2$(1) (Litres/min.)	Predicted Max $\dot{V}O_2$(2) (Litres/min.)	Predicted Max $\dot{V}O_2$(3) (Litres/min.)	Observed Max $\dot{V}O_2$ - Predicted Max $\dot{V}O_2$ as a % observed Max $\dot{V}O_2$		
					(1)	(2)	(3)
R.M.M.	3.38	2.83	2.86	2.91	16.3	15.4	13.9
J.T.H.	3.38	2.68	2.90	2.74	20.7	14.2	18.9
D.S.O.	4.54	3.73	3.70	3.52	17.8	18.5	22.5
F.E.G.	4.82	4.46	4.90	4.22	7.5	+1.7	1.2
W.J.S.	3.57	2.89	3.30	2.70	19.0	7.6	24.3
R.W.L.	2.92	2.27	2.30	2.68	22.3	21.2	8.2
I.R.F.	3.01	2.59	2.60	2.96	14.0	13.6	1.7
C.F.J.R.	3.84	3.30	3.50	3.18	14.1	8.9	17.2
A.F.M.	5.43	4.36	4.75	4.46	19.7	12.5	17.9
A.E.C.C.	3.29	2.63	2.60	2.74	20.1	20.8	16.7
Mean	3.82	3.17	3.34	3.21	17.15	13.10	14.25
S.D.	0.83	0.72	0.89	0.65	4.36	7.66	8.43

The maximum heart rate of the athletes is significantly different from the remainder of the group ($p < .05$). The coefficient of correlation relating the two variables is significant at the 0.1 level. This would suggest that training does have a slight but definite effect on the maximal attainable heart rate. Of itself, the error likely to be produced in estimation of Max $\dot{V}O_2$ by this factor is small. Extrapolating the EHR/$\dot{V}O_2$ line to a population mean value of 190 beats/min. instead of actually observed maximum value results in an error of approximately $\pm$ 274 cc./min. at the 95% confidence level. This is not significantly different ($p > 0.05$) from the error to be expected from the random day-to-day variation in the measurement of EHR and $\dot{V}O_2$ and is less than the error produced by the asymptotic nature of the heart rate curve.

3.4.4. The prediction of Max $\dot{V}O_2$ from submaximal values of EHR and $\dot{V}O_2$

The combined effect of the errors which are likely to occur due to the relationship of EHR to $\dot{V}O_2$ previously outlined on the prediction of Max $\dot{V}O_2$ is shown in table VII. As is to be expected, the magnitude of the error due to the combined effect of the asymptotic nature of the heart rate curve and inter-subject variability in the maximum heart rate attainable, precludes an accurate and realistic estimation of Max $\dot{V}O_2$. Using the mean maximum heart rate of the group, 190 beats/min., the error is 17.15 $\pm$ 8.72%.

Table VII also indicates that if the regression equation is not calculated and only single measurements of heart rate

and $\dot{V}O_2$ are used after the method of Åstrand and Rhyming (1954), this error is likely to increase. This is hardly surprising, especially when one considers the additional premises on which the method is based., viz. that all straight lines have a common point which at zero $.O_2$ uptake levels to 60 beats/min., thus Max $\dot{V}O_2$ can be determined by either extrapolating the EHR/$\dot{V}O_2$ line through a single point to heart rate of 195 beats/min. or reading the Max $\dot{V}O_2$ as twice the value of $\dot{V}O_2$ at an EHR of 128 beats/min. Reference to table VI shows that in fact the heart rate at zero $\dot{V}O_2$ levels varies from 38 to 64. Thus, the Åstrand-Rhyming procedure of drawing a straight line through three points, one of which is assumed (195 beats/min.), one biassed (60 beats/min.) and the other (observed) subject to random error is not valid and therefore unlikely to yield accurate results.

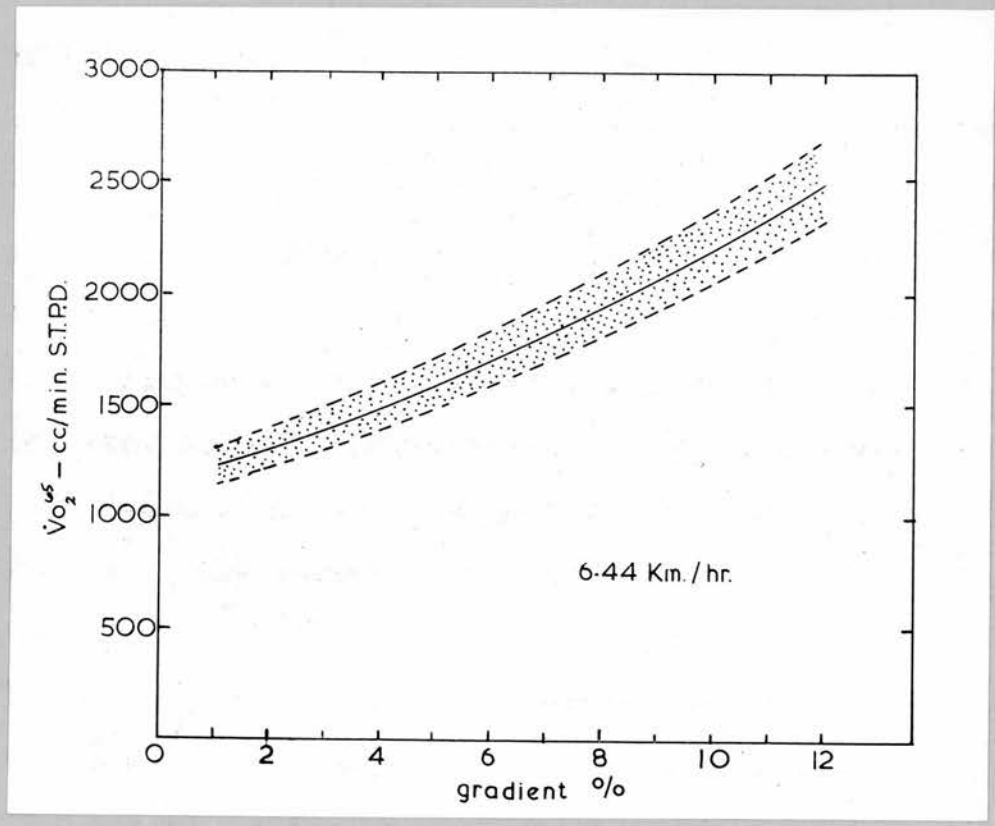
The method of Asmussen and Molbech does attempt to overcome one of these difficulties by actually incorporating the resting heart rate into their prediction. This does seem to reduce the mean error of the method, but the general scatter of the results is increased. The resting heart rate is an extremely variable function even under the most carefully standardised conditions (cf. table VIII, page 97). During the routine estimation of Max $\dot{V}O_2$ the method may give rise to an increased accuracy of prediction purely by chance, due to the resting pulse being over- rather than under-estimated. This, however, can hardly serve as a recommendation for its use as a more reliable method.

3.4.5. Prediction of $\dot{V}O_2$ from work load

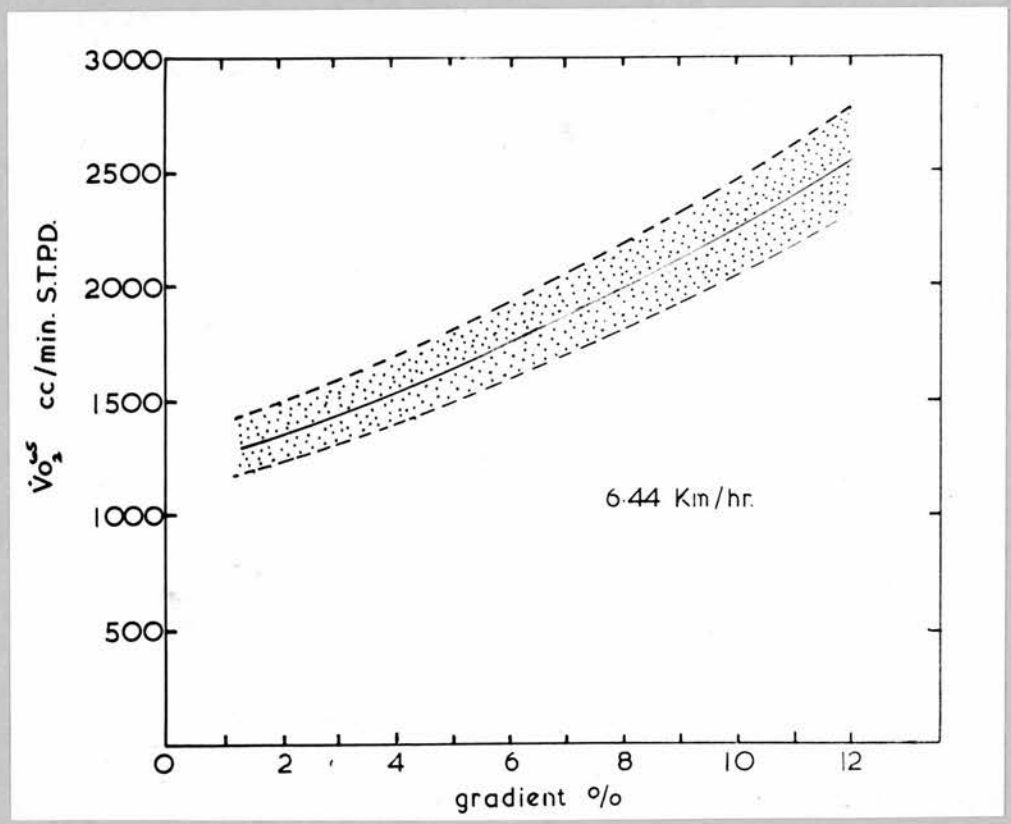
The aim of this part of the study was to try and discover the accuracy by which $\dot{V}O_2$ could be estimated during routine measurement of Max $\dot{V}O_2$ by simply substituting values of work rate into a mean population equation of the form $y = ax + b$ where $y = \dot{V}O_2$ and x = work rate. Since in practice each individual will have his own line representing the relationship between the two variables, the feasibility of the method will depend on the inter-variation between one individual and another around a population mean being of the same order of magnitude as the intra-variation within a given individual.

In order to investigate this problem the data given in table IV was re-analysed in the following way: 1) Homogeneity of variance was achieved by performing a log transformation on the original data (Bartlett's test for homogeneity of variance was applied to the transformed data using x^2 as the test criterion. This was not significant, i.e., homogeneity of variance could be assumed.) 2) A straight line was fitted to the transformed data and tested for goodness of fit by means of analysis of variance using Snedecor "F" as test criterion. (In both sets of data this revealed that the variation between gradients not accounted for by regression was not significant and that the fitting of straight lines was justified.) 3) Ninety-five per cent confidence limits for the lines were calculated. These were converted to numbers (by taking antilogs) and plotted in fig. 30.

fig. 30. Relationship of O_2-uptake ($\dot{V}O_2^{65}$ S.T.P.D.) to work load (see text).



a) Intra-subject variability.



b) Inter-subject variability.

The results indicate that the differences between intra and inter subject variability are small and the mean straight line for relating $\dot{V}O_2$ and work rate in a given individual does not differ significantly for the population mean straight line for the group at the 95% level of confidence. Thus, the procedure of estimating $\dot{V}O_2$ of the individual from single measurements of work rate using a population $\dot{V}O_2$/work rate diagram would be justified for routine assessment. Using the formula $\log_{10} \dot{V}O_2 = 0.070 + 0.028$ WR (i.e., $\dot{V}O_2 = 10^{[0.070 + 0.028\ WR]}$; it can be shown (fig. 30) that any predicted value of $\dot{V}O_2$ will lie within $\pm$ 9% of the actual value at the 95% level of confidence.

3.5. Discussion

It has been argued previously that the accurate prediction of Max $\dot{V}O_2$ from EHR and $\dot{V}O_2$ data collected at submaximal loads will depend on: 1) the linear relationship between the two variables holding up to and including maximal levels of work so that maximum heart rate and oxygen intake are reached at the same level of exercise; 2) all subjects under consideration must be able to reach a similar maximum heart rate; and 3) if $\dot{V}O_2$ is to be predicted from work rate and not measured, the variance of $\dot{V}O_2$ around a population mean $\dot{V}O_2$/work rate line must be of the same order of magnitude as the day-to-day random variability of directly determined $\dot{V}O_2$ for any given individual.

Clearly, 1) and 2) are not strictly valid for human subjects. They produce a variable error which precludes the accurate assessment of Max $\dot{V}O_2$ in man. However, the error from 2) is small in comparison with 1) and insignificantly different from that to be expected from normal random day-to-day variation in the assessment of Max $\dot{V}O_2$. The major limitation to the direct prediction of Max $\dot{V}O_2$ from heart rate and $\dot{V}O_2$ data collected at submaximal levels of exercise would seem to be the asymptotic nature of the heart curve. Extrapolation of the EHR/$\dot{V}O_2$ line to an observed or assumed maximal pulse will result in a gross under-estimation of an individual's capacity to consume oxygen at maximum rates of work.

The possible reasons for this asymptotic relationship are not altogether clear. Åstrand (1960) rightly criticised

similar findings of Wyndham et al. (1959) on the grounds that the data was collected at an altitude of 6000' on subjects extremely light in stature. An asymptotic heart rate curve and low maximal pulse (the mean value for Wyndham's four subjects was 178 beats/min. which is low for young healthy adults) have been shown by Åstrand and Åstrand (1958) in subjects suffering from tissue hypoxia. However, since Edinburgh is a lowland city and the maximum heart rate and average stature of my subjects are closely in accord with figures given by Åstrand and Rhyming (1954) in their original investigation, these criticisms are unlikely to be applied to my results.

The uptake of oxygen is governed quantitatively by the equation:

$\dot{V}O_2$ = heart rate x stroke volume x A - $\dot{V}O_2$ difference

ml./min. beats/min. ml./beat vol.%

If it be accepted that above a heart rate of 120 beats/min. no further rise in stroke volume takes place (Saltin, 1964) then at higher rates of work a further increase in $\dot{V}O_2$ will depend solely on the heart rate and arterio-venous difference. There is no direct evidence in man to say which of these two parameters is exhausted first, but the fact that in this experimental investigation at near maximal effort, a rise in $\dot{V}O_2$ has been shown to occur without any perceptible change in the heart rate, does suggest that a small additional amount of oxygen can be extracted from the circulating blood by the working muscles. This could occur in ~~two possible~~ the following ways~~;~~ ~~either~~ ~~(1)~~ by a further increase of O_2 unsaturation of mixed venous

blood, ~~or (2) desaturation of arterial blood. Both these mechanisms are known in man,~~ This mechanism is found ~~the former~~ more especially in patients suffering from mitral stenosis who find difficulty in increasing their heart output during exercise (Donald et al., 1954), but presumably a similar compensatory mechanism might occur in health during conditions of severe physical stress due to the almost complete shutdown and diversion of blood flow from areas of low O_2 extraction (e.g., kidney viscera - see Wade and Bishop, 1962) to the working muscle where the rate of oxidation is proceeding at a high rate. This could lead to a greater over-all O_2 extraction from the blood circulating within the body which could result in an increased A - $\dot{V}O_2$ difference and therefore a rise in O_2 uptake without a concomitant increase in cardiac output.

~~Indirect evidence for the latter mechanism occurring in man was first given by the studies of Bannister and Cunningham (1954) and Nielsen and Hansen (1937). They both showed that by increasing the partial pressure of oxygen in inspired air, arterial hypoxaemia could be reduced and performance during exhaustive exercise improvided, a finding consistent with the possible occurrence of desaturation. Recently, direct determination of oxygen saturation by Rowell et al. (1964) have confirmed this view. They found that during a three-minute run to exhaustion, arterial oxygen saturation fell from 95.8% at rest to 93.4% and 91.4% in a sedentary group before and after training and to 85.2% in endurance athletes.~~

An increase in oxygen uptake by ~~either or both of these~~ this

two mechanisms at near maximal performance would give rise to a disproportionate rise in $\dot{V}O_2$ compared with heart rate transforming a hitherto straight EHR/$\dot{V}O_2$ line into an asymptotic curve.

Unfortunately, there is no physiologically valid solution to this problem, apart from fitting a precise curve to the data, but in practice this would be extremely difficult, since it would involve repeated measurements of $\dot{V}O_2$ and EHR at all levels of exercise on every subject under consideration and this is open to some criticisms and drawbacks as the direct determination of Max $\dot{V}O_2$. The only possible alternative would be to apply an arbitrary correction factor to compensate for the "bias" in estimating the "true" Max $\dot{V}O_2$ value. This may simply be achieved by extrapolation of the EHR/$\dot{V}O_2$ line to a heart rate some 20 beats higher than the mean population figure of 190 beats/min., but inter-subject variability in the magnitude of the error due to the asymptotic nature of EHR curve limits the accuracy of the procedure to $\pm$ 14%. (Using work rate as an indirect measure of $\dot{V}O_2$ this error is likely to be increased by $\pm$ 4%).

Thus, even when applying a large standard correction factor, the method remains of limited value and provides only a rough guide to the individual ability to perform at maximum effort. For accurate analysis of physical working capacity in man there is no alternative but to measure Max $\dot{V}O_2$ directly.

CHAPTER 4

Aerobic capacity for prolonged work

4.1. Physiological background

In Chapter 3 working capacity was defined in terms of oxygen utilization and energy expenditure and it was argued that the ultimate measure of a person's capacity for exercise was the maximum rate of oxygen he could transport and utilise in unit time. Thus, measurement of a person's maximum oxygen uptake is undoubtedly one of the most important determinants of his capacity to perform work, but for many forms of human activity a definition involving maximal criteria is often unhelpful (because it involves risk and a certain amount of co-operation from the subject) and unrealistic. For, even well trained athletes can only endure exercise at maximum rates for a few minutes and one is rarely interested in such short periods of work. This is particularly true in the industrial situation, where more often the focus is on the highest rate of submaximal work which is within the capacity of the individual to perform for prolonged periods without undue fatigue, rather than short bursts of maximal effort. Thus, a definition of working capacity in these terms would often be of greater practical value.

It has now been well established that when a subject starts exercising, though he immediately begins to expend energy at a rate proportional to his muscular work, his oxygen intake rises more slowly, but during light-to-moderate

exercise it soon levels off after 1-2 minutes and remains at this level for the duration of the work period. During the latter part of such exercise most bodily functions remain constant. The O_2 supply reaches a level which is just sufficient to provide by the oxidation the energy required to carry out the work, no excess lactate appears in the blood (Jarvell, 1928; Owles, 1930, Friedmann et al., 1945, Lundin and Ström, 1947; and Asmussen, 1950) and thus the various internal equilibria of the body are maintained close to their resting conditions. The deficit which is incurred at the start of exercise is repaid rapidly during the recovery period, giving rise to a small O_2 debt.

It is only when exercise reaches certain critical levels that the initial lag in the cardio-respiratory adjustment becomes more marked and prolonged, the rate of supply of O_2 no longer meets the requirements of the working muscles, carbohydrate becomes incompletely oxidised, anaerobic metabolism begins and excess lactate accumulates in the circulating blood (Margaria et al., 1933; Cotes, 1955; Holmgren, 1956; Holmgren and Ström, 1959; and Harris et al., 1962). This is removed during the recovery period, giving rise to increased respiration and subsequent O_2 debt. If exercise is increased beyond these levels, the supply of O_2 lags further and further behind muscle demands. The proportion of energy derived from anaerobic mechanisms increases with concomitant rises with rate of accumulation of excess lactate in the blood and repayment of O_2 debt.

Only at levels of work in which the cardio-respiratory

adjustment to exercise is sufficient to maintain the transport of O_2 at a rate commensurate with the muscle needs and is characterised by the absence of anaerobic metabolism can men be expected to work for prolonged periods (Åstrand, 1956). Thus, the point beyond which a lactacidaemia and large O_2 debt begins to occur not only defines the highest intensity which may be met by purely oxidative processes, but it may be said to characterise a person's aerobic capacity for prolonged physical work.

Unfortunately, the determination of the level of O_2 uptake at which anaerobic metabolism occurs is not a simple procedure even in the most well-equipped laboratories. For it has now been generally accepted, following the series of papers by Huckabee (1958 a, b, c) that though an apparent relationship exists between O_2 debt and blood lactate concentration, the latter variable is not an accurate quantitative measure of anaerobic metabolism, since its concentration can be increased in the absence of tissue hypoxia by such procedures as hyperventilation and pH changes of the blood. Only that fraction of total lactate change (i.e., "excess lactate") which is not subject to non-hypoxic errors is closely related to anaerobic metabolism and O_2 debt and this must be calculated from the total lactate/pyruvate changes in the body.

This is an extremely laborious time-consuming procedure; it involves the almost continuous sampling of blood and is therefore unsuitable for routine laboratory field application. An indirect measure of the level of O_2 uptake at which

anaerobic metabolism begins to occur during exercise of increasing intensity, would have enormous advantages as the basis of a test to assess the capacity of the individual for prolonged work, but so far no-one has been able to develop a suitable index to the stage of being reliable and physiologically acceptable.

"A priori" reasoning would suggest that if such an index could be developed, it must come from one of the factors which govern the transport of oxygen from the outside on to the site of its utilisation in the body. These factors are:

1. Pulmonary ventilation.
2. Distribution of gases within the lungs and the diffusion rate of oxygen from the alveoli to the blood.
3. Oxygen capacity of the blood as it is reflected in the haemoglobin concentration and the degree of dissociation of the oxyhaemoglobin in the tissues.
4. Cardiac output.
5. The functional state of the peripheral blood vessels leading to and from the working muscles, the rate of blood flow through the muscles and the oxygen diffusion from muscle capillaries to the tissues.
6. The biochemical efficiency of the enzyme systems within the muscle concerned with oxygen uptake and release of energy for mechanical work.

The relative importance of these different factors during severe exercise is still a matter for debate amongst

physiologists. In disease, each factor may impair performance and set its upper limits, but in healthy adults the picture may be very different.

Åstrand (1956) in a recent review has gathered together most of the relevant information and under normal conditions of health it seems unlikely that factors 1 - 3 play a decisive part in limiting an individual's capacity for exercise.

Certainly, the results outlined in the previous chapter show that pulmonary ventilation cannot be limiting in the sense that an increase of ventilation makes more oxygen available to tissues. Most subjects were able to increase their maximum ventilation at maximum effort without perceptibly changing their Max $\dot{V}O_2$. A similar argument can be applied to diffusing capacity (D_{LO_2}), which is known to increase during exercise of increasing severity (Bøje, 1933), and to be higher in athletes than non-athletes (Bannister et al., 1960). It has also been shown to improve in sedentary subjects following a period of training (Newman et al., 1962). Nevertheless, if D_{LO_2} is a limiting factor in exercise one would expect that breathing O_2 enriched air would increase $\dot{V}O_2$ during severe work, but this has not been consistently found. The effect of O_2 on improved performance is only seen at high concentration (Bannister, Cunningham and Douglas, 1954) which suggests that it is not due to better conditions of diffusion, but rather to some other specific influence on the circulatory, or possibly, central nervous systems.

Anaemia is a common cause of reduced working capacity and as such needs no further discussion, but it is probable

that in the normal healthy adult the level of haemoglobin in the circulating blood is more than sufficient during maximal exercise to cope with the transport of the increased supply of oxygen from the pulmonary capillary bed to its site of utilisation within the working muscles. Thus, the key to the measurement of capacity for prolonged physical work would seem to rest with circulatory rather than respiratory factors. These are more difficult to discuss separately, for though it has often been postulated that the major effects of training on performance are due to an increased biochemical efficiency of oxidative processes and blood flow within the working muscle, we have limited experimental evidence. Certainly, in patients suffering from mitral stenosis and who are unable to increase heart output, the increased efficiency of O_2 extraction in the tissues constitutes an important compensatory mechanism (Donald et al., 1954). Exercising of limbs in which the blood supply has been reduced results in lower $\dot{V}O_2$, increased O_2 debt and ischaemic pain. In normal exercise, work with the legs is known to produce higher $\dot{V}O_2$ than similar work with the arms (Christensen, 1932) and the highest Max $\dot{V}O_2$ has been recorded in athletes using large muscle groups on activities such as skiing (Christensen and Högberg, 1950) which all suggests that oxygen uptake is limited by local blood flow through the muscle's vascular bed. However, more recent work of Mitchell et al. (1958) and Saltin (1964) show that this is not true. Indeed, the latter author has shown

conclusively that, provided the exercise was severe, the diffusion area of the muscle mass engaged in leg work was more than sufficient to take on the maximum volume of oxygen provided by the heart. His evidence further shows that the oxygen volume available to the tissues (maximal cardiac output x O_2 content of the arterial blood) becomes the limiting factor during maximal exercise and "cardiac output becomes decisive with constant haemoglobin concentration (oxygen content of arterial blood)".

If we accept Saltin's finding, therefore, might not a causal relationship exist between the time course of cardiac output changes during exercise and the onset of anaerobic metabolism in man? Further, since stroke volume has been shown to increase over a very narrow range of O_2 uptake at the commencement of effort (Asmussen and Neilsen, 1955; Wade and Bishop, 1962; and Åstrand et al., 1964) might not these changes in heart output be reflected in the pattern of heart rate response during the early phase of exercise of increasing intensity?

In comparison to the wealth of information which has accumulated on the exercise heart rate, comparatively little attention has been given to the earliest phase of exercise during which the heart rate increases from its resting towards its steady state level.

Since the classical work of Bowen (1904) it has been known that during moderate-to-heavy exercise the primary abrupt rise in heart rate is often followed by a slower secondary rise to the steady state value. This delay in

reaching a steady state has been shown to occur at lower levels of exercise in the untrained compared with trained subjects (Christensen, 1931; Taylor, 1941; and Harris, 1957) and in elderly subjects compared with young healthy students (Harris and Thompson, 1958) to be more pronounced in all groups during severe work and often giving way to a continuous rise in pulse rate throughout the exercise period. Some authors (Christensen, 1931; Müller, 1950; and Karrasch and Müller, 1951) have postulated that this continuous rise in heart rate might reflect the inadequacy of the oxygen supply to working muscles, whilst others (Le Blanc, 1957; and Brouha et al., 1963) have suggested that it might be a sign of fatigue and cardiac strain. However, despite these suggestions only one attempt, to the author's knowledge, that of Harris and Porter (1958) has been made to relate changes of the heart rate during the early phase of exercise quantitatively to O_2 consumption by the working muscles. They characterised the secondary rise in heart rate by calculating the "pulse deficit" at the beginning of exercise at eight different rates of work and showed that it remained at near zero until a rate of oxygen consumption of 1.8 - 2.0 litres was reached. Beyond this point both "pulse deficit" and oxygen debt rose steeply.

The experiments to be described aim to confirm and extend the work of Harris and Porter by defining more precisely 1) the course of the heart rate and O_2 consumption and respiratory exchange during exercise of graded intensity; 2) the nature of the relationship between the tachycardia of exercise and

occurrence of anaerobic metabolism as indicated by the contraction and repayment of O_2 debt; and 3) to decide on the feasibility of using the time course of the heart rate changes during early exercise to measure the actual aerobic capacity of the individual. Part of this work has already been published appears as an appendix to this thesis on page 108.

In order to define a relationship between two variables using human material, an accurate assessment must be made of the intra-subject variability. Single measurement of the parameters at a number of work rates on a large group of subjects only allows an assessment of inter-individual differences about a mean. It does not allow precise definition in the individual case. To overcome this difficulty repeated measurements on the same individual over a wide range of exercise intensities must be made. This allows the appropriate mathematical curves to be fitted to the data and their goodness of fit tested by rigid statistical techniques. The variability can be defined by the use of 95% confidence limits. However, though this approach does allow the interrelation between the physiological factors under consideration to be studied more accurately, it does have the disadvantage that it imposes a limitation on the subjects which can be studied at any one time. This investigation, therefore, was confined to two subjects of widely differing work capacities.

4.2. Procedure

The anthropometrical details of the two subjects studied are given in table XXI. A.F.M. is an athlete of international standing. He first represented his country (Scotland) in June, 1964 and later that year was selected to run for Great Britain in the 10000m. event at the Tokyo Olympic games. He is probably the fastest man of his age in this country at 3000m. and 5000m. distances. During the twelve-month period beginning March, 1964, his training schedule was phenomenal: he covered a total distance of nearly 4000 miles and averaged 75 miles/week. His best times for the mile and 3000m. distances are 4 min. 0.6 secs. and 8 min. 11.8 secs. respectively. The present world records (1965) for these distances are 3 min. 54.4 secs. and 7 min. 49.2 secs. respectively.

C.T.M.D., though interested in physical activity was, at the time of measurement, of sedentary habit. He was studied three times a week over a two-month period at each of seven levels of exercise (3.22 km./hr., 4.83 km./hr. and 6.44 km./hr. on the level and 6.44 km./hr. up gradients of 3%, 6%, 9% and 15%.) He reported to the laboratory in the post-absorptive state at 8.30 a.m. on each of the experimental days. The preliminary period was rigidly standardised and consisted of a warm-up period (6.44 km./hr. on the level for 10 min.) followed by a 45-minute rest period, during which time the necessary electrodes and respiratory apparatus was fitted. The measurement of basal metabolic rate was then carried out and at minus one minute the subject was asked to stand,

seconds were counted aloud until zero time, at which the treadmill was started and exercise was performed at the chosen gradient. At six minutes the treadmill was stopped, the chair replaced on the treadmill and the subject was allowed to recover in the sitting position.

In order to try and construct both the exercise and recovery $\dot{V}O_2$ curves, each experiment was repeated four times at the upper four levels and three times at the lower two levels of work, the collection of expired air being staggered by fifteen seconds on the former and sixty seconds on the latter occasion (table XXI). At the highest rate of work (15%), though four experimental runs were attempted, the subject found great difficulty in performing the work, which resulted in only one run being successfully completed. The data from this single experiment, which should be treated with caution, has been given in table XXI and indicated separately in figs. 34, 35 and 36.

A.F.M. was studied in a similar manner, but unfortunately, he was a busy young man. His training schedule occupied 21 hours a week and he was in his final (examination) year at the University. Consequently, he could only afford a limited time to take part in this investigation and this meant a curtailment of the originally-planned programme. The experiments were carried out over a one-month period directly following his return from the Tokyo Olympic games. He was studied at five levels of work (6.44 km./hr. up 9%, 12%, 15% and 18% gradients, and 11.27 km./hr. up 12% gradients). He reported to the laboratory at various times during the day

in the post-absorptive state. The preliminary period was again rigidly standardised and followed the same pattern as outlined for C.T.M.D. Expired air was collected during the first four and last two minutes of exercise at each gradient and for thirty minutes during the recovery period of all except the lowest level of work (table XXI).

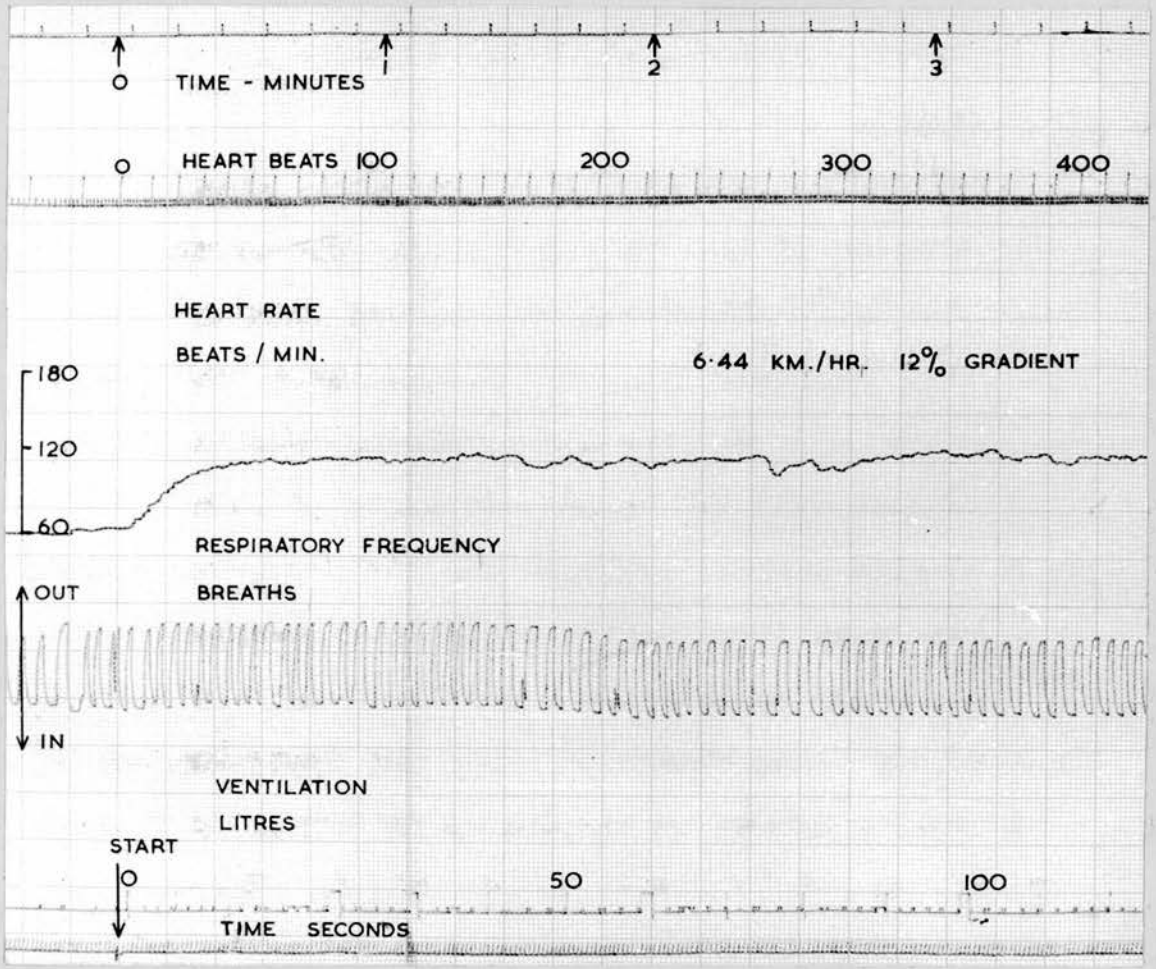


fig. 32. Experimental record taken during exercise. From above downwards: heart beats and heart rate recorded by cardiotachometer and linear instantaneous ratemeter, respiratory frequency recorded by thermistor, and ventilatory volume recorded via a relay attached to CD_4 gasmeter.

4.3. Methods

The heart rate, respiratory frequency and ventilatory volume were monitored continuously in the manner previously described (page 13) and recorded directly on to paper using an Eddison-Swann four-channel pen recorder. A portion of an actual experimental record is shown in fig. 32.

Expired air

Expired air was collected into small Douglas bags using the technique of Hill et al. (1924). The errors which might arise from the collection, storage and analysis have already been noted (Appendix I). The dead space of the apparatus was reduced to a minimum and carefully flushed out with the subject's expired air before the start of each experimental run. A rigorous and exacting tap-turning technique was practised many times during preliminary sessions in order to avoid error which might occur from small volumes of expired air being channelled into the wrong Douglas bag. Each tap was turned at one-minute intervals to coincide with the subject's moment of expiration. The maximum theoretical error using this technique to measure $\dot{V}O_2$ at various respiratory frequencies was calculated to be not greater than $\pm$ 5%. All samples were analysed by the Haldane method. Duplicate samples were required to agree within 0.05 vols. %.

O_2 deficit and debt

The accurate measurement of O_2 deficit and debt is difficult, for 1) at low levels of exercise both deficit and repayment are small and often the error due to random

error too large for effective analysis; 2) at work loads at or near maximum performance the cumulative debt from the failure of the O_2 transporting system to meet the demands of tissues may prevent a steady state and thus result in a gross under-estimation of O_2 deficit; and 3) a final source of error is the difficulty of establishing a steady resting base line from which to compute the excess O_2 consumption during the recovery period. Resting metabolic rate is one of the most difficult variables even under the most rigidly standardised laboratory conditions. Further, following severe exercise it is always difficult to assess whether recovery O_2 uptake has returned to the pre-resting baseline. This is especially true of long recovery periods when the subject becomes restless and $\dot{V}O_2$ fluctuates accordingly.

In order to overcome these difficulties, recovery O_2 uptake was measured over the time intervals recommended by Hill et al. (1924) for light, moderate and severe exercise. Repeated measurements of O_2 uptake over these periods allowed curves to be fitted to the data as previously outlined and recovery was assumed complete when the value of the recovery asymptotic coincided with the resting baseline. The latter was defined in terms of the mean $\pm$ 2 standard deviations from 15 and 6 separate pre-exercise resting O_2 consumptions in subjects C.T.M.D. and A.F.M. respectively. For comparative purposes, O_2 deficits at the higher rates of work were neglected.

TABLE VIII.

Resting O_2-uptake

Subject	Number of Observations	$\dot{V}O_2$ 65 c.c./min. S.T.P.D.		
		Range	Mean	S.D.
C.T.M.D.	15	201-248	222.6	14.9
A.F.M.	4	230-252	245.0	10.1

TABLE IX.

Exercise O_2-uptake curves of the form $y = a + be^{-cx}$, where y and x have the designation as in the text, together with test of goodness of fit based on Snedecor "F" value, and probability (P) of given value being exceeded.

Gradient %	Speed (km./hr.)	a	b	c	$F(2,N-3)^P$	P
0%	3.22	596.33	-356.23	-1.7632	44.24	< .001
0%	4.83	784.46	-537.73	-1.2079	110.91	< .001
0%	6.44	1145.36	-896.82	-1.8056	382.03	< .001
3%	6.44	1388.97	-1145.55	-1.7108	977.88	< .001
6%	6.44	1705.60	-1472.52	-1.3927	1118.22	< .001
9%	6.44	1995.25	-1725.99	-1.3562	383.36	< .001

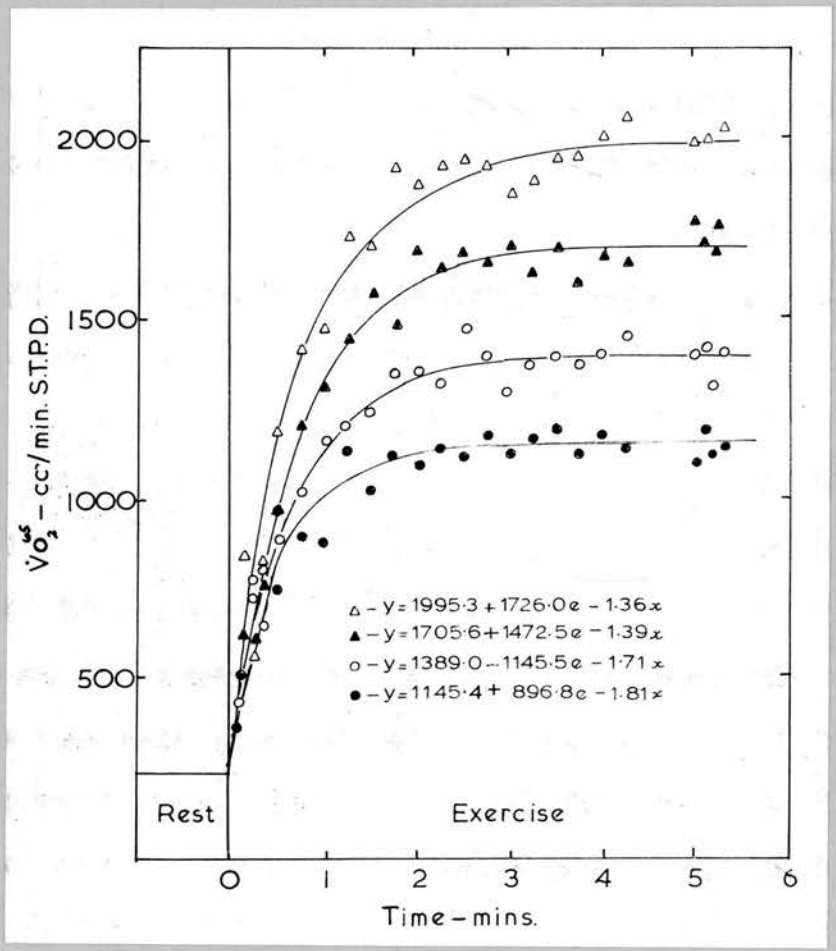


fig. 33. Time course of O_2-uptake ($\dot{V}O_2^{65}$) changes during early exercise. The curves of the form $a + be^{-cx}$ were constructed from data taken from four separate experimental periods at the different levels of work.

4.4. Results

4.4.1. Respiration

4.4.1.1. O_2-uptake at rest

Table VIII summarises the measurements of resting O_2-uptake for the two subjects. The mean value for A.F.M. would appear to be some 20 cc. higher than that recorded for C.T.M.D. The difference, however, is not statistically significant.

4.4.1.2. O_2-uptake during the transition from rest to work

The $\dot{V}O_2$ data for both subjects is given in table XXI. The large number of measurements of $\dot{V}O_2$ made during the transition from rest to exercise on subject C.T.M.D. allowed mathematical curves of the form $y = a + be^{-cx}$ to be fitted to the data. They were tested for goodness of fit by means of the variance-ratio test using Snedecor "F" as the test criterion. The relevant equations, together with the values of F and the probability of their being exceeded if the hypothesis (of exponential rise) under test is true, are given in table IX. They indicate two points: 1) that indeed the curves are a very satisfactory fit to the data, and 2) at the higher rates of work there is a progressive delay in reaching the asymptotic $\dot{V}O_2$ value. This can be seen more clearly in fig. 33, which gives a plot of the individual curves at the various work rates against time. Indeed, the actual $\dot{V}O_2$ points at 6% and 9% gradient appear to show an initial rapid rise and small overshoot followed by a slower climb to a steady state value. The differences in the mean $\dot{V}O_2$ values between the second and fifth minute of exercise

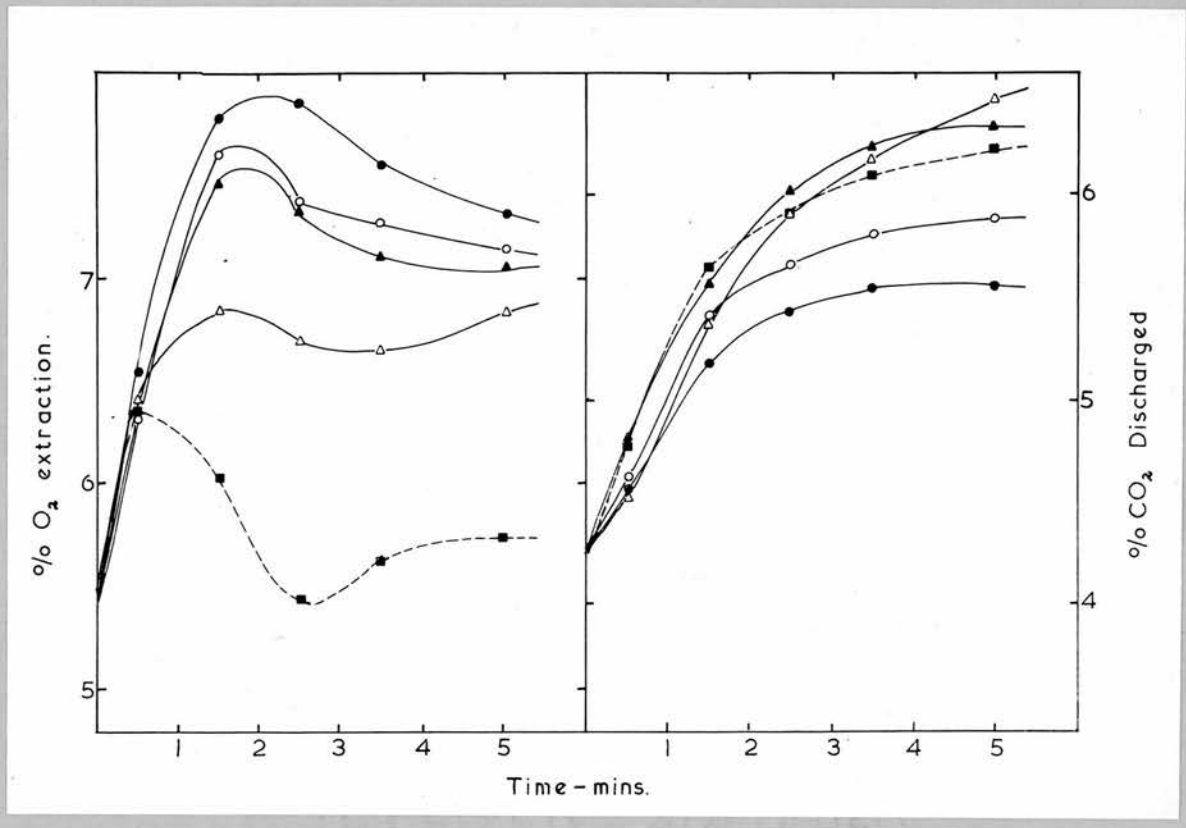


fig. 34. Oxygen Extraction (OE) and carbon dioxide discharged (CO_2D) during exercise at five work levels: 6.44 km./hr. on the level ●——●; up 3% o——o; 6% ▲——▲; 9% △——△; and 15% ■——■.

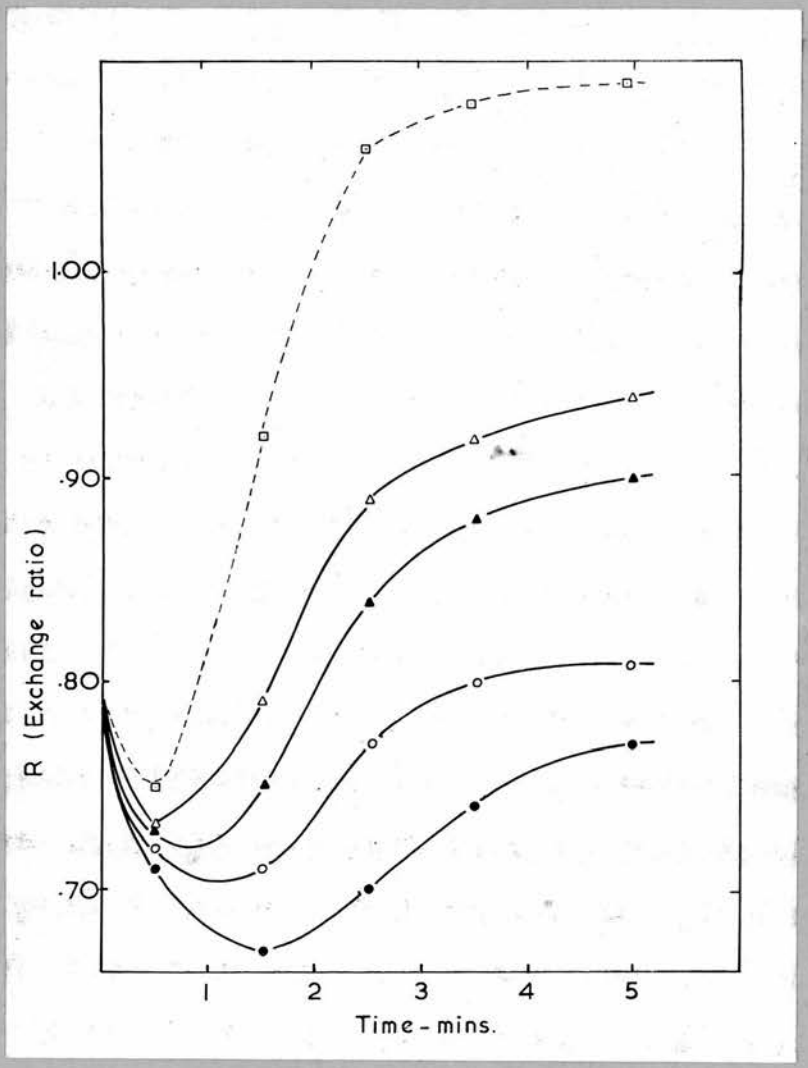


fig. 35. The time course of the respiratory exchange ratio (R) during exercise at five work levels.

on the level and up a 9% gradient were 39 cc. and 171 cc. respectively. Similar rises in O_2-uptake after the second minute of exercise in sedentary subjects have been noted by Henry (1951), Henry and De Moor (1956) and Royce (1962). The rise in $\dot{V}O_2$ during exercise was brought about by an increase in both ventilation and O_2 extraction. The latter, however, was more marked during the early phase of work and was almost entirely responsible for the rapid increase in $\dot{V}O_2$ during the first few seconds of exercise. The % O_2 extraction from the inspired air was initially maximum within the first half-minute of exercise and often reached remarkably high values (in excess of 8%) during the lighter work loads (table XXI and fig. 34). Beyond the second minute at the lowest levels of exercise, as ventilation increased towards the steady state value, the O_2 extraction fell; thus, it was always less in the fifth, compared with the second minute of exercise. At the two higher rates of work, however, this primary fall in O_2 extraction was more often followed by a slow rise which lasted throughout the exercise period (fig. 35) The increase in O_2 extraction beyond the three minutes was small; however, the final values recorded during the fifth minute of exercise still remained significantly below the figures obtained during the first half-minute of work.

This transient lag in ventilatory response during which little CO_2 was blown off by the lungs, combined with the high extraction of O_2 to produce a characteristic pattern of exchange ratio (R) changes during the first few minutes of exercise (fig. 35). At all grades of work R fell immediately

TABLE X.

Recovery O_2-uptake curves of the form $y = a + be^{-cx}$, where y and x have the designation as in the text, together with test of goodness of fit based on Snedecor "F" value and the probability (P) of given value being exceeded.

Gradient %	Speed (km./hr.)	a	b	c	$F_2(2,N-3)$	P
0%	6.44	221.76	782.54	0.9664	178.70	< .001
3%	"	250.84	978.62	1.1219	397.6	< .001
6%	"	241.96	1414.62	1.1953	101.00	< .001
9%	"	268.30	1102.40	0.5602	38.55	< .001
15%	"	257.31	1172.43	0.5095	185.26	< .001

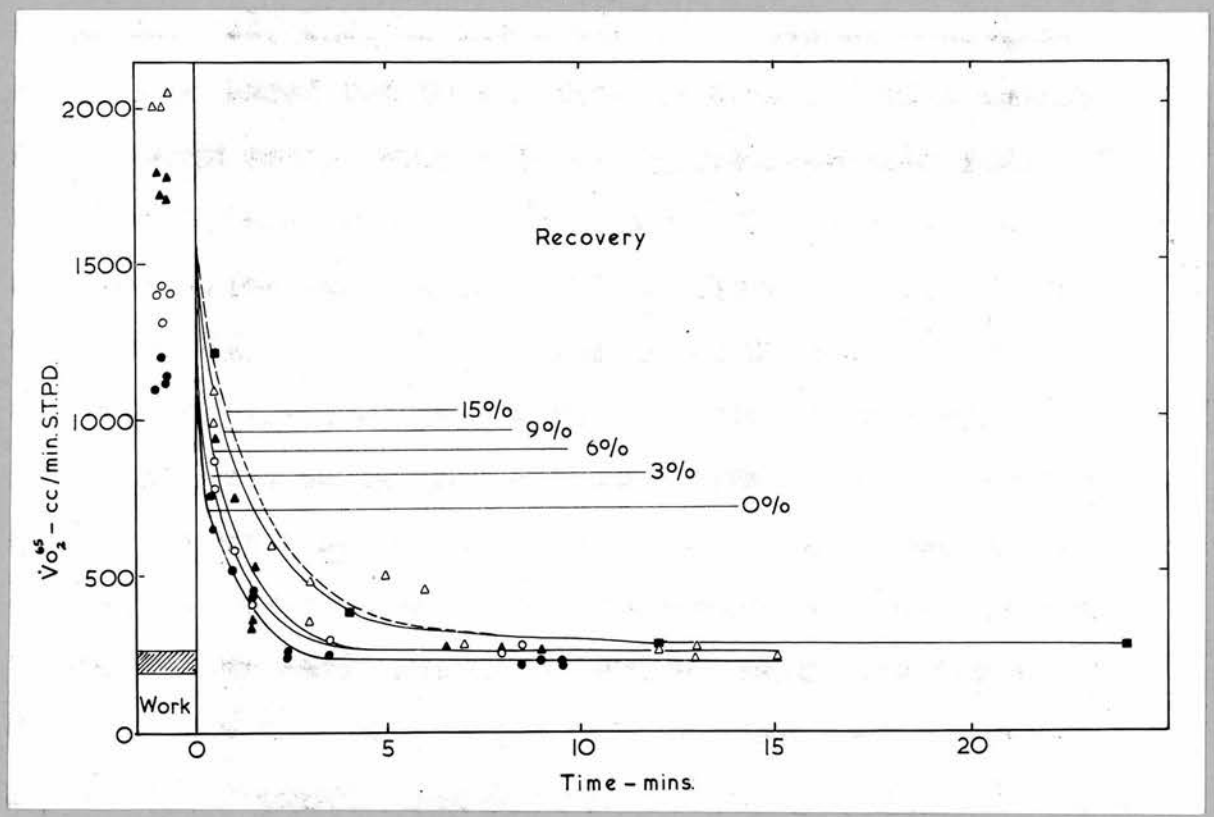


fig. 36. O_2-uptake during work and recovery. (Symbols same as fig. 34).

at the onset of exercise to reach a minimum value during the second minute and then showed a marked rise. Maximum values were reached during the final minute of exercise.

4.4.1.3. O_2 uptake during the recovery from exercise

Curves of the form $y = a+be^{-cx}$ were fitted to plots of recovery $\dot{V}O_2$ against at each of the five upper work loads in subject C.T.M.D. They are shown in fig. 36. The equations, together with the test of goodness of fit based on the Snedecor "F" value and probability (P) of a given value being exceeded is given in table X. From the curves, recovery appears to be complete within 3 mins. at 0% at work rate corresponding to a $\dot{V}O_2$ of 1141 cc./min. and 5 mins. at 3% ($\dot{V}O_2$ = 1389) and 6% ($\dot{V}O_2$ = 1764) respectively. At 9% ($\dot{V}O_2$ = 1995) and 15% ($\dot{V}O_2$ = 2465) though O_2 uptake reached within 20 c.c. of the resting baseline within 12 mins. it remained at this level throughout the thirty-minute recovery period. Even after two hours this figure had only been reduced by 10 cc. This amount may represent a continued repayment of O_2 debt or may be due to other factors such as an elevated body temperature, an increase in circulating adrenaline (Gray and Beetham, 1957), increased oxidation of fat and an altered electrolytic balance (Passmore and Johnson, 1960) which cause a general disturbance in bodily functions and shift of the pre-resting baseline. At the highest levels of exercise this elevation in O_2 uptake is quite small, relative to the total recovery O_2 intake and does not influence the values for total debt to an appreciable extent.

During the first minute of recovery CO_2 was eliminated rapidly from the body. This, combined with a low % O_2

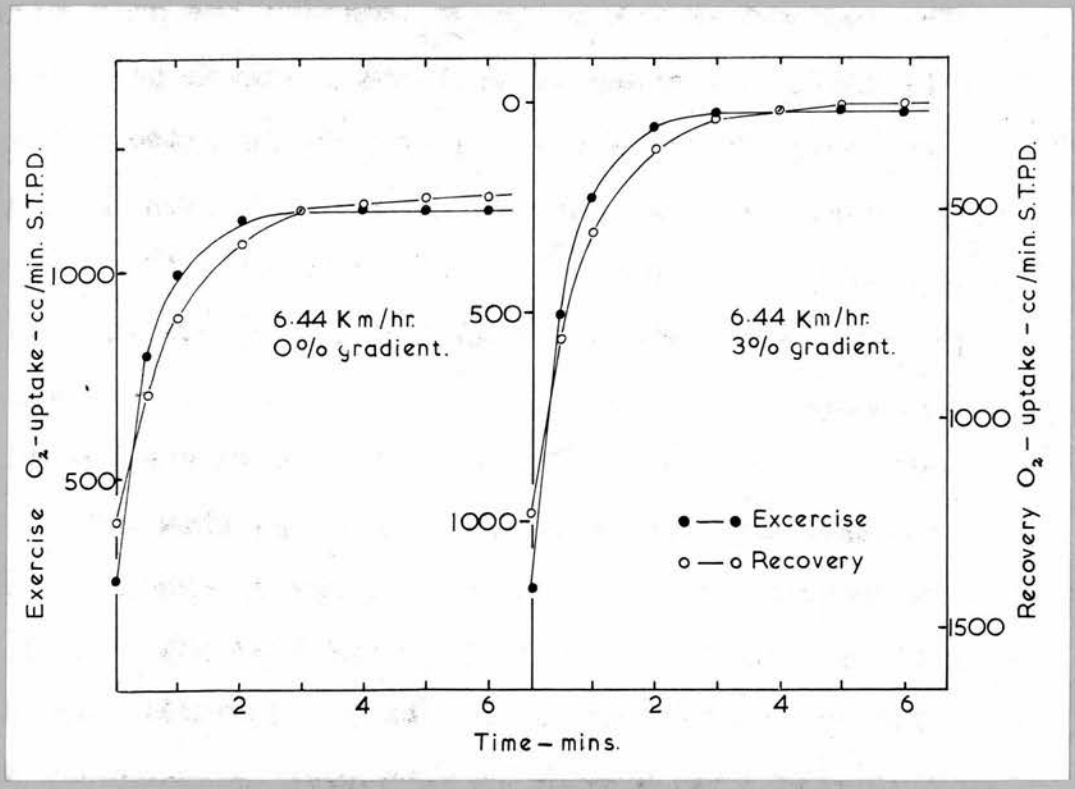


fig. 37. Comparison of the O_2-uptake curves during work, ●——● and recovery o——o at two exercise levels. Note that the recovery scale is inverted.

extraction from the inspired air to produce a pattern of RQ changes is completely the reverse of that seen during the initial stages of exercise (table XXI). As recovery progressed, however, CO_2 was retained, R often falling below resting values.

4.4.1.4. The relationship between O_2 debt and deficit

The individual values for O_2 deficit and debt are given in table XXII. In order to meet the criteria previously outlined, only debts contracted and repaid below a work rate corresponding to an oxygen uptake of 2.0 Litres/min. have been compared. The ratio of deficit to debt ($^{R}/_{D}$) would seem to indicate a simple quantitative relationship between the two variables. The correlation is r = 0.947. In addition, the plot of the mean O_2 uptake curves at work rates of 1141 cc./min. and 1389 cc./min. (fig. 37) show that the deficit portion of the curve are nearly an exact mirror image of each other and thus indicate that any slight quantitative discrepancies between the actually measured size of deficit and debt must be due to small differences in the resting and post-exercise baseline. These results are strictly in accord with Hill's original theory of O_2 debt and would seem to refute more recent suggestions of Alpert, Kayne and Haslett (1958) that no such quantitative link existed between the initial deficit of exercise and excess O_2 consumption of recovery.

It is perhaps also worthy of note that the absolute values of O_2 debt performance as calculated in this investiga-

TABLE XI.

Resting heart rate.

Subject	Number of Observations	$\dot{V}O_2$ 65 cc./min. S.T.P.D.		
		Range	Mean	S.D.
C.T.M.D.	16	57 - 78	70.12	5.51
A.F.M.	5	41 - 47	43.00	2.45

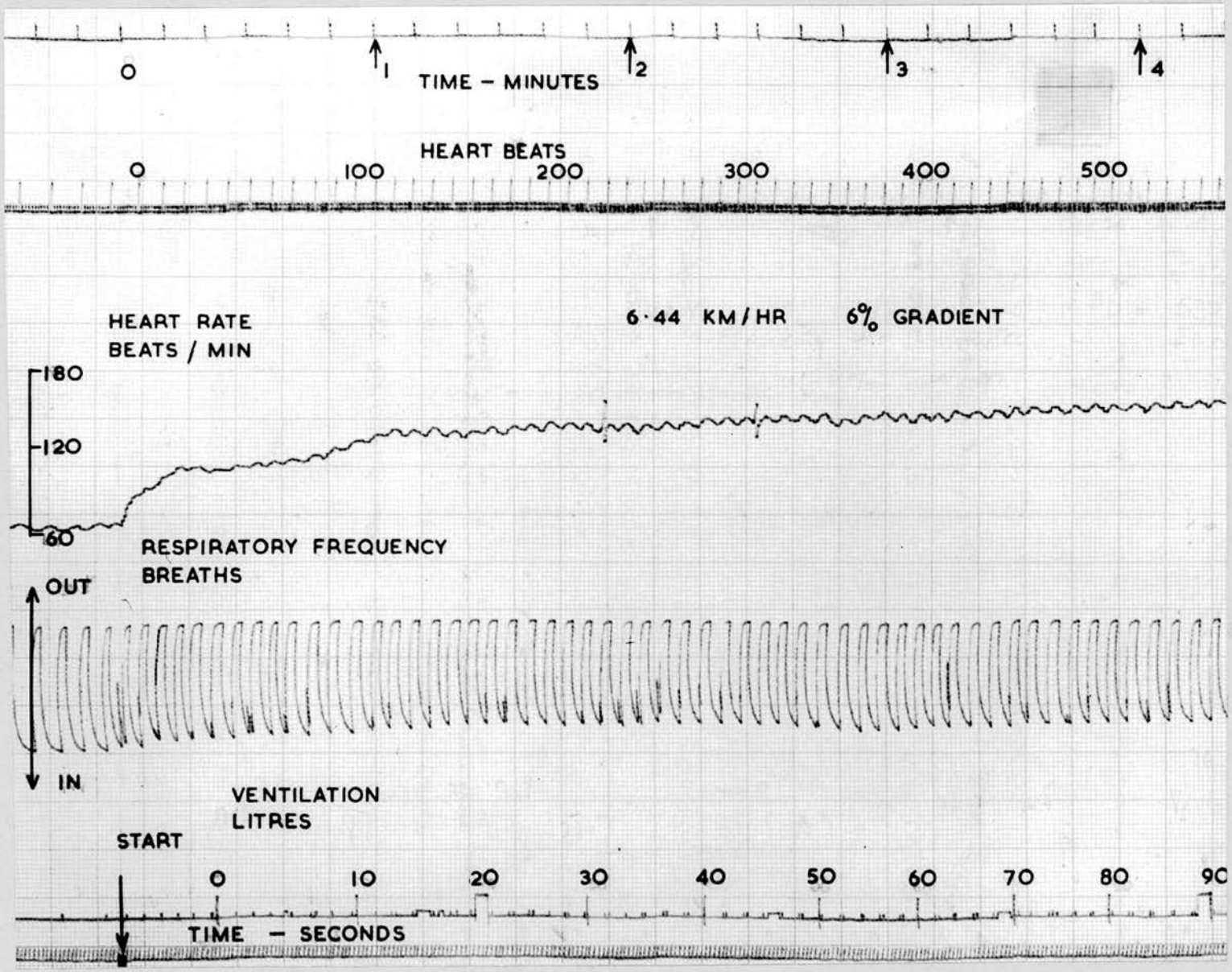


fig 38. The heart rate during the transition from rest to exercise.

see text

tion are much lower than those envisaged by Hill and the earlier workers in the field. If the plots of O_2 debt against $\dot{V}O_2$ shown in figures 41 and 42 are extrapolated to the individual subject's Max $\dot{V}O_2$ values of approximately 9 litres and 7 litres are obtained for the athlete and non-athlete respectively, these are some 6 - 8 litres lower than those quoted by Hill for work involving maximum effort. They are, however, closely in accord with the more recent observations of Margaria et al. (1963).

4.4.2. The heart rate

4.4.2.1. The resting heart rate

The resting heart rate values for both subjects are given in table XI. They show a difference of some 30 beats/min., the mean value for C.T.M.D. being 70.2 $\pm$ 5.51 beats/min. and A.F.M. 43 $\pm$ 2.45 beats/min.

4.4.2.2. The course of the heart rate during exercise

The heart rate rose immediately at the onset of exercise in both subjects. During light exercise this primary abrupt rise accounted for some 95-100% of the total rise seen during the exercise. The steady state heart rate was thus always reached within the first minute of exercise. As the exercise intensity was increased, however, this simple pattern of heart rate change was no longer maintained. In subject C.T.M.D., exercise was increased beyond a certain level corresponding to $\dot{V}O_2$ of approximately 1700 cc./min., a more gradual rise in rate of 3-3.5 minutes' duration began to appear which was separated from the initial increase by a

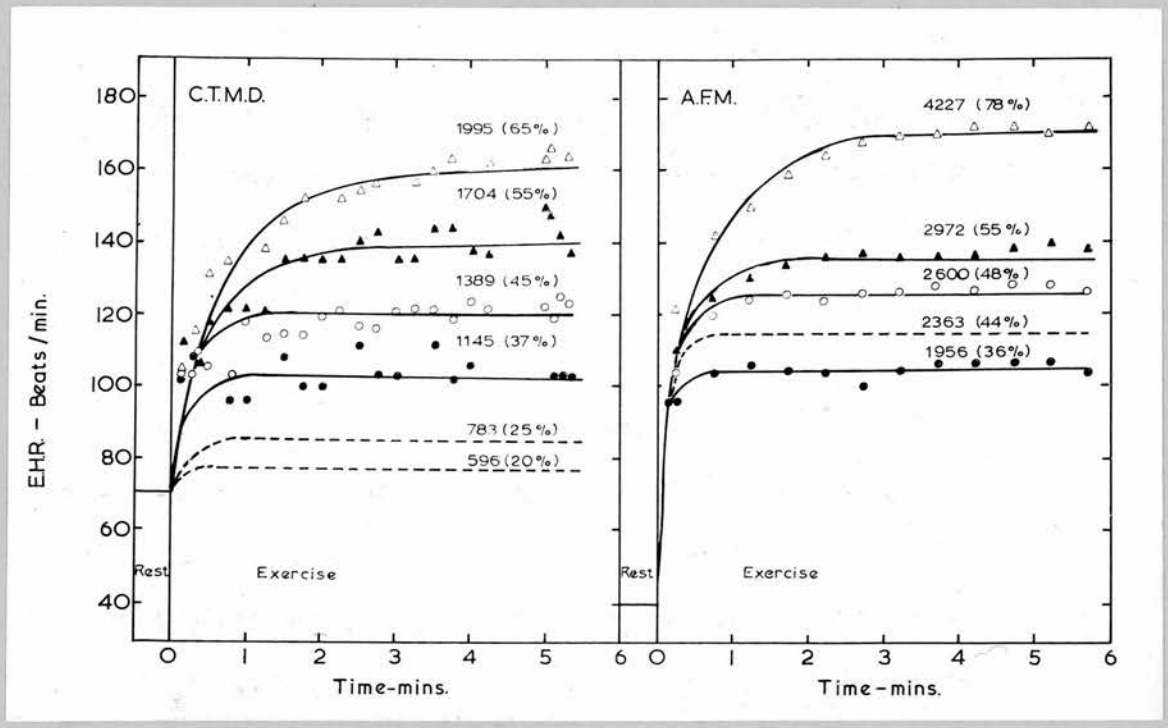


fig. 39. The heart rate during the transition from rest to exercise for the two subjects. The steady state values of $\dot{V}O_2^{65}$ are given and expressed as a % of the Max $\dot{V}O_2^{65}$ (enclosed brackets). The curves are of the form $y = a + be^{-cx}$. The relevant equations together with the tests of goodness of fit based on the snedecor "F" value are given in table IX.

plateau during which the heart rate remained constant (fig. 38). This secondary rise became more pronounced as the intensity of exercise was increased at 9% ($\dot{V}O_2$ = 2000 cc.) the heart rate appeared to climb throughout the exercise period.

In the athlete similar changes were observed, but at very much higher rates of work. A small but definite secondary rise lasting some two minutes was first seen at a work load corresponding to a $\dot{V}O_2$ of approximately 3000 cc./min. (fig. 39).

In order to compare the heart rate records of the two subjects more precisely, the data from the original records was extracted and treated in the same way as previously outlined for O_2 uptake in section 4.4.1.1. The individual values of the heart rate were plotted against line and curves of the form previously described for O_2 uptake were fitted to the data. They were tested for goodness of fit by analyses of variance. The relevant equation and "F" values are given in table XII and the heart rate graphs are shown in fig. 39. They show that indeed the time course of the heart rate changes for both subjects are remarkably similar and in fact, become almost identical if expressed in terms of relative (as % of Max $\dot{V}O_2$) rather than absolute work load. The effect of the secondary rise is reflected in the time taken for the heart rate to reach its asymptotic value. At work loads below approximately 45% Max $\dot{V}O_2$ in the sedentary subject and 55% in the athlete, the asymptotic

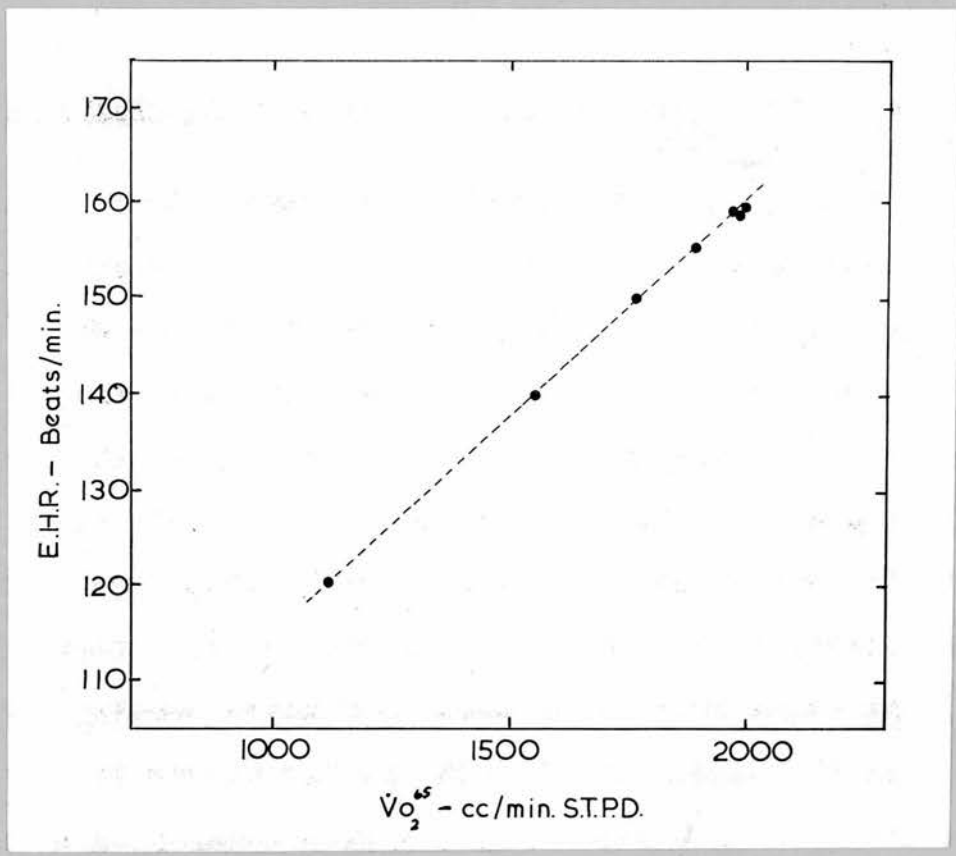


fig. 40. Heart rate (EHR) in relation to O_2-uptake ($\dot{V}O_2^{65}$ S.T.P.D.) during the 1st to 5th min. of exercise at a work rate corresponding to approximately 2 Litres/min.

value of the heart rate is reached within 1 - 1½ minutes. However, beyond these critical levels of work the asymptote is reached more slowly and a decided lag in the heart rate response appears. The linear relationship of this delayed rise in heart rate to oxygen consumption is indicated in fig. 40.

4.4.2.3. <u>The heart rate in relation to aerobic capacity for work</u>

In order to characterise the changes in heart rate previously outlined and relate them to the aerobic capacities of the two subjects, the total area above the curve was calculated from the equations given in table XII and plotted together with the exchange ratio (R) oxygen debt against $\dot{V}O_2$ in figs. 41 and 42. In both subjects it will be seen that with increasing exercise the O_2 debt curve rises in almost rectilinear fashion and the calculated and R values stay near resting conditions until work load corresponding to 1.7 Litres/min. in the sedentary subject and 3.0 Litres in the athletes. Thereafter, all three variables rise steeply calculated in almost linear fashion with work load. Only at the highest rate of work in subject C.T.M.D. does this relationship begin to break down. The PD declines as the heart rate nears its maximum value.

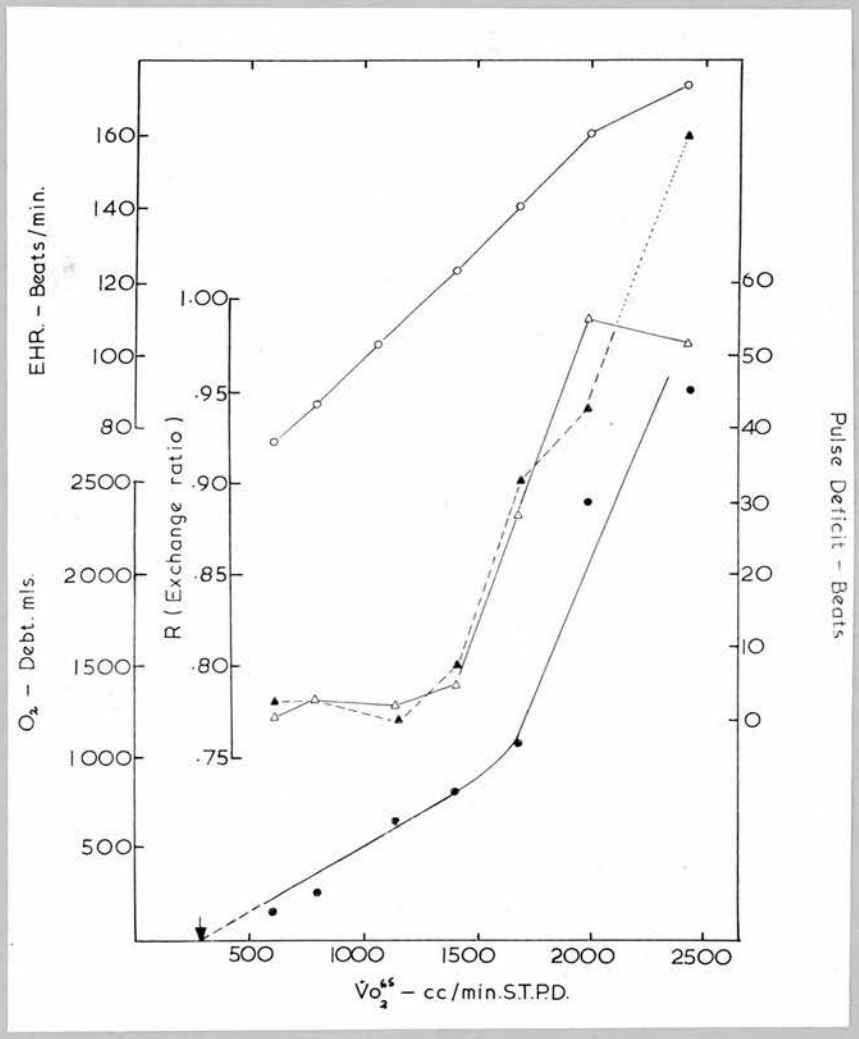


fig. 41. from above downwards:

o–o The mean heart rate (EHR) during the 4th to 6th minute.

△–△ The pulse deficit (PD) as defined in the text.

▲---▲ The respiratory exchange ratio (R) during the 4th to 6th minute of exercise.

●–● O_2 debt. The line has been extrapolated (---) to an observed mean resting O_2-uptake value indicated by an arrow on the abscissa.

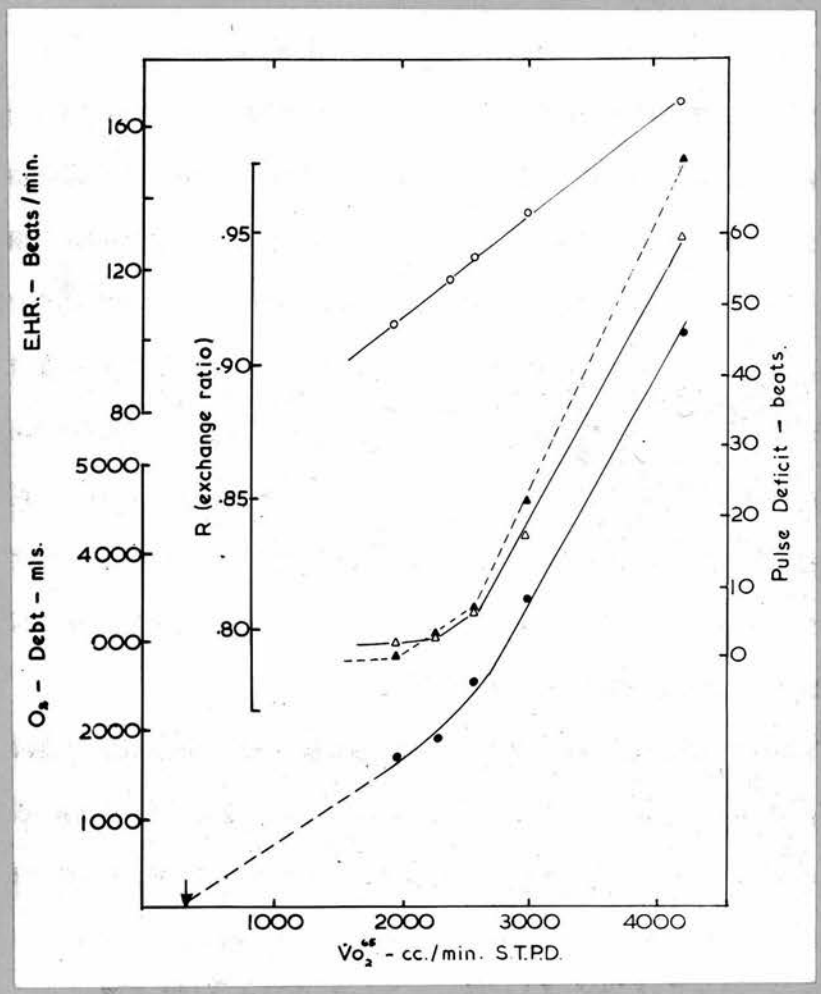


fig. 42. See fig. 41.

4.5. Discussion

The O_2 debt curves are remarkably similar to those given by Margaria et al. (1933) and Knuttgen (1962). They found that the end of the rectilinear phase of the O_2 debt curve at approximately 1.5 Litres/min. and 2.5 Litres/min. in a non-athlete and athlete respectively corresponded closely to the point at which excess lactate began to accumulate in the circulating blood. Thus, though lactate was not measured directly in my experiments from the behaviour of the O_2 debt curves and the exchange ratio (R) there would seem excellent grounds for assuming that the point at which the calculated PD shows a distinct rise marks the beginning of a metabolic acidosis and thus characterises the aerobic capacity of the two subjects and essentially confirms and extends the work of Harris and Porter (1958).

The underlying reasons and mechanisms thought to be responsible for these changes and the degree of association between the heart rate during early exercise and the onset of anaerobic metabolism is less clear. The factors which might be responsible for a delayed rise in heart rate during exercise are numerous. They have, however, been reviewed recently by Asmussen and Nielsen (1955). Of the known determinants of heart rate it would seem unlikely that emotion, temperature, or stimuli from working muscle due either to rapidity of movement or the accumulation of anaerobic metabolites could account for the observed changes, since 1) Both subject were well versed and "trained" in performing experiments on the motor-driven treadmill: throughout all the experiments they were complete-

ly relaxed and no emotional tachycardia was seen (cf. fig. 38). 2) The rise in oral and rectal temperature has been shown to be small during the first six minutes of exercise (<0.2°C) and it is doubtful if so small a rise could account for a cardiac acceleration of nearly 25 beats/min., nor in any case could it account for the differences between the two subjects and the fact that acceleration did not continue beyond the 4th minute at 6%, or the 3rd minute at 18% in C.T.M.D. and A.F.M. respectively. 3) A reflex cardio-acceleration due to increased movement of the legs during the early stages of exercise can be discounted since stride rate remained constant after the first thirty seconds of exercise. 4) The effect of muscles working under partly anaerobic conditions could produce a secondary rise in heart rate. This is clearly an attractive theory, but there is no evidence in man or animals that metabolites can either directly or indirectly affect the heart rate (Mansfield, 1910; Asmussen et al., 1940) and in any case it would be difficult to explain why the EHR in my experiments undergoes no apparent change from aerobic to anaerobic levels of work. Indeed, "a priori" reasoning would suggest that anaerobic metabolites are not a cause but a result of O_2 deficiency within the working muscles. Further, the close association between $\dot{V}O_2$ and heart rate from the first to fifth minute of exercise would seem to indicate that the stimulus which initiates heart rate and keeps it going at working level is closely related to the work intensity and degree of demand

of the tissues for oxygen, and totally unrelated to the degree of anaerobiosis within the working muscles.

On this basis one might assume that once an O_2 need has been created and a stimulus to heart output has been effected, provided the muscles can readily accept the O_2 offered to them (see Åstrand, et al., 1964), the degree of anaerobic metabolism will depend upon the rapidity by which the output of the heart can adapt to meet the requirements of the working muscles. It would seem, therefore, reasonable to postulate (since stroke volume increase has been shown to be an unimportant concomitant of all except the very lowest grades of work) that the PD reflects the deficit in cardiac output in the early stages of exercise and the existence of the deficit determines the occurrence of anaerobic metabolism, the accumulation of excess lactate in the blood and the subsequent contraction of an O_2 debt. Thus, the beginning of lactate levels of exercise will be marked by a delayed rise in heart rate and sharp increase in PD. Beyond this, the author is not prepared to speculate at present.

The results do indicate, however, that of all the criteria to be derived from the heart rate during the transition from rest to work, that the PD might be used to characterise the aerobic capacity of the individual and thus, in the light of previous discussion, might be used to form the basis of a simple, safe rational test of an individual's capacity for prolonged work. In order to investigate this problem further, the data from a previous investigation (Chapter 3), together with the original data of Harris (1957)

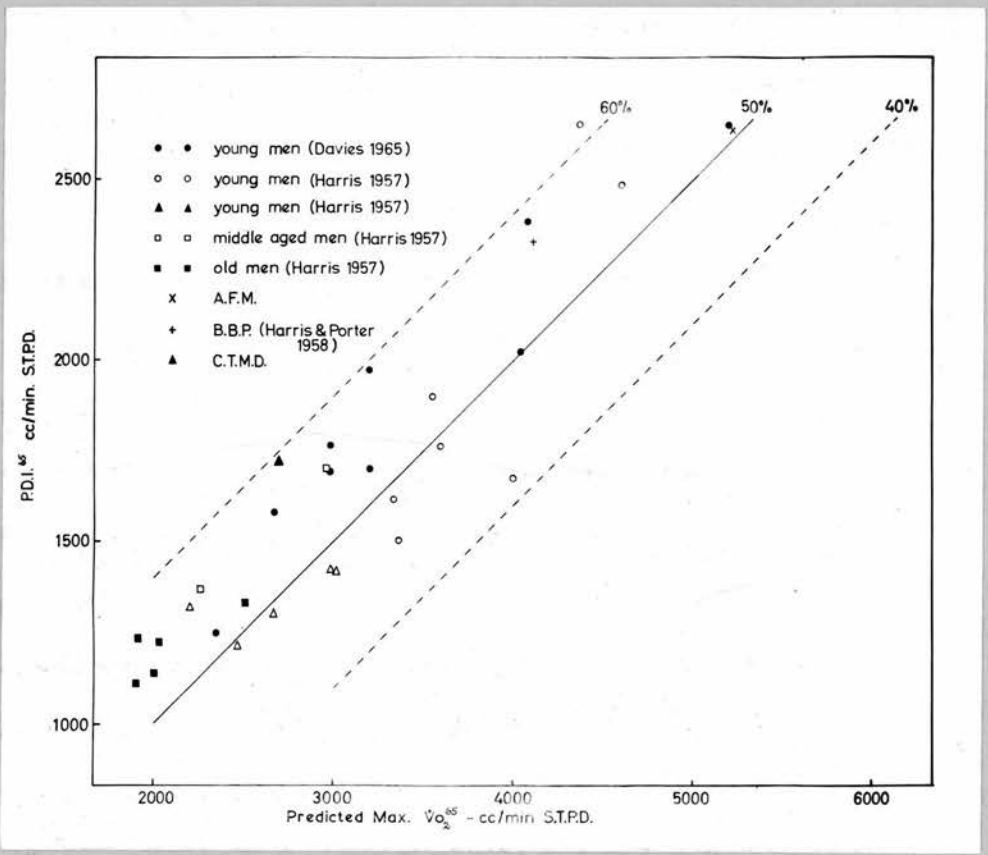


fig. 43. Relationship of Pulse Deficit Index (PDI^{65}) to predicted maximum oxygen uptake for subjects of different ages, sex and fitness levels. The lines for 40%, 50% and 60% Max $\dot{V}O_2$ are given.

collected from an athlete, 6 female and 6 male students, 2 men aged 35 and 47 years and 4 healthy old men aged 70 - 79 years was anslysed and index derived from the pulse deficit of early exercise. The PDI^{65} (which was taken on the lowest $\dot{V}O_2$ - STPD corrected to body weight of 65 kg. at which the PD showed a decided upward swing - see appendix II page 858), has been plotted against a predicted value of the Max $\dot{V}O_2$ (AC^{65} - after the method of Åstrand, 1960) in fig. 43.

In all the well-trained subjects the marked rise in PD occurs at 55-60% of their predicted Max $\dot{V}O_2$. For the less fit individuals the figure is slightly less, being nearer 45-55%. These figures are in close agreement with the corresponding values for the accumulation of excess lactate given by Strydom et al. (1962) and Williams et al. (1964) obtained from similar material. In addition, it will be noted that these figures hold good even when individuals of different age groups are compared. This is consistent with the data of Robinson (1938) and Åstrand (1960) who have shown that, provided comparable levels of O_2 uptake are used and comparison is made with Max $\dot{V}O_2$, the level of lactate in the blood is independent of sex and age and depends only on the fitness of the individual. Thus, it would seem reasonable to suggest that the PDI^{65} gives a valid indication of the level of work at which anaerobic metabolism begins and therefore could be used to fix the capacity of the individual for prolonged work.

The procedure for determining PDI^{65} is simple and safe, but there are two factors that could possibly interfere with its accurate assessment during routine application: The

emotional tachycardia which often precedes effort in untrained subjects and the unreliability of pulse counts taken at lower levels of exercise if only single experiments are performed. Both these factors could give rise to difficulties when trying to establish the level of exercise at which the PD shows a marked rise. When exercise is light, an emotional tachycardia may give rise to a negative PD and when more severe, make the PD less positive, thus giving rise to a falsely high PDI^{65}. The unreliability of pulse counts below a heart rate of 125 beats/min. could affect the PDI^{65} in either direction.

An emotional tachycardia can be easily detected and prevented by allowing the subject to perform a series of dummy runs to become accustomed to the procedure. By this means, too, the errors from the measurement of heart rate at low exercise intensities can be reduced to a minimum (table XXII and fig. 39). Thus, apart from its rationalisation on theoretical grounds, which is at present speculative, the PDI^{65} would seem to have several advantages over conventional indices based on the heart rate and would certainly seem worthy of further investigation and development as a possible basis of simple, safe and rational test of a person's capacity for aerobic work.

SUMMARY AND CONCLUSIONS

Maximum oxygen intake

An analysis of the heart rate - O_2-uptake curves of ten subjects was presented in relation to the over-all limitations of predicting Max $\dot{V}O_2$ under the following headings i) errors due to random variations in the measurement of heart rate and $\dot{V}O_2$ under normal standard laboratory conditions; ii) non-linearity in the heart rate - O_2-uptake time and iii) the inability of all subjects under consideration to reach approximately the same maximum pulse. It was shown that:-

1. The major drawback to all methods which rely on the extrapolation of the heart rate - O_2-uptake line to an assumed maximum pulse was the asymptotic nature of the heart rate curve. This was shown to introduce bias of the order of 652 ± 365 cc./min. (at the 95% confidence level) in the estimation of Max $\dot{V}O_2$ and thus precluded an accurate and realistic prediction of a subject's performance capacity from data collected at submaximal levels of work.
2. In comparison, the error due to the inter-subject variability in the maximum pulse levels attainable was small. The use of population mean maximum pulse resulted in an error of approximately $\pm$ 274 cc. This was shown to be insignificantly different from the error to be expected from random day-to-day variation in the measurement of heart rate and O_2-uptake.
3. The underlying reasons which might be responsible for the asymptotic nature of the heart rate curve and an

alternative formula for predicting Max $\dot{V}O_2$ was discussed. It was concluded that if an accuracy greater than $\pm$ 15% was required, then there was no alternative but to measure Max $\dot{V}O_2$ directly.

Aerobic capacity for work

The heart rate and respiration during the transition from rest to exercise in relation to the aerobic capacity for work was studied in an Olympic athlete and a healthy male subject. It was shown that:-

4. The behaviour of the heart rate and respiration during the early phase of exercise was remarkably similar in both subjects. As exercise was increased in intensity, a level of exercise was reached at approximately 1700 cc./min. in the non-athlete and 3000 cc./min. in the athlete, beyond which the exchange ratio (R) began to show its first marked rise, the O_2 debt curve departed from its rectilinear form, the heart rate began to exhibit a slower secondary rise to a delayed steady state value and thus the total heart beat deficit (PD) during the first four minutes of exercise began to increase sharply from near zero levels.

The underlying mechanisms responsible for and the implications of these observed changes were discussed. It was suggested that the heart rate during early exercise might be used to characterise the aerobic capacity of the individual.

5. In order to investigate this problem further an analysis of healthy subjects of different ages and sex was presented. It was shown that the delayed rise in heart rate only became marked at levels of exercise corresponding to 55-60% of

predicted Max $\dot{V}O_2$ in well-trained subjects and 45-55% predicted Max $\dot{V}O_2$ in less fit individuals. It was thus independent of sex and age, and related only to the fitness of the individual.

6. The possible use of an index derived from the adaptation of the heart rate to exercise (PDI^{65}) as a basis for a simple rational test of capacity for aerobic work was discussed.

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CHAPTER 5

Concluding remarks

5.1. Acknowledgements

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Appendix 1

THE RAPID SAMPLING, STORAGE AND ANALYSIS OF EXPIRED AIR

THE RAPID SAMPLING, STORAGE AND ANALYSIS OF EXPIRED AIR

CONTENTS

Introduction

This study arose as a result of the experimental investigations described in chapter 4. In order to try and examine the time course of O_2-uptake changes during the early phase of exercise, it was necessary to develop methods for the rapid sampling and (due to little technical help being available) the subsequent storage and analysis of expired air.

These three factors constitute one of the most important problems in the field of respiratory and metabolic physiology. It is well known, for instance, that error can be introduced by faulty technique and the diffusion of carbon dioxide, especially when rubber bags are used, but surprisingly few systematic investigations of the whole problem have been undertaken. Undoubtedly, in many laboratories where measurement of respiratory function is routine, studies have been carried out, but the fact remains that very little data is available in their final published work.

For convenience, this study has been divided into three parts. In part 1 the rapid fractional sampling of expired air has been investigated and discussed in relation to the magnitude of error that is involved under normal physiological conditions; in part 2 an assessment is made of the various storage containers available for both the short and long term storage of expired gas materials; and in part 3 a comparison has been presented between a more modern, rapid (physical) method of gas analysis and the conventional Haldane (chemical) technique.

1. The rapid sampling of expired air

1.1. Introduction

The simultaneous changes in oxygen extraction and ventilation which are known to occur during early exercise make it difficult to collect a true representative of mixed expired air by direct means. Most authorities are agreed that a large chamber must be placed in the respiratory circuit to allow complete mixing of the expired gas before sampling can take place, but little quantitative information is available regarding the precise dimensions of the chamber or whether true one-minute samples of expired air can be withdrawn from it.

Bock et al. (1928) have suggested the use of an 8-litre chamber in series with Tissot gasometer, and though they claim that rapid fractional samples of expired air can be withdrawn, their paper only gives one table of nine comparisons between their method and the standard Tissot, four of which differ by more than 0.1 vols. %. Nevertheless, their work has often been quoted and used as a basis for most respiratory systems designed to collect and measure expired air (Cunningham et al., 1957); only one group of workers (Donald et al., 1954) to the author's knowledge have claimed that the precaution of a chamber is unnecessary. They sampled directly from a sidearm placed in the respiratory tubing leading from the subject to the gasometer.

It was in order to gain more information of rapid sampling during the transition from rest to exercise (see

chapter 4) in general, and the extent to which a mixing chamber was necessary in particular, that this study was undertaken.

The study necessitated the rebuilding of Bock's original chamber with certain modifications to allow for a wider range of volumes and simultaneous side-arm sampling to be investigated. Since a large Tissot was not available, the standard Douglas bag method of collecting and sampling expired air was used throughout the investigation.

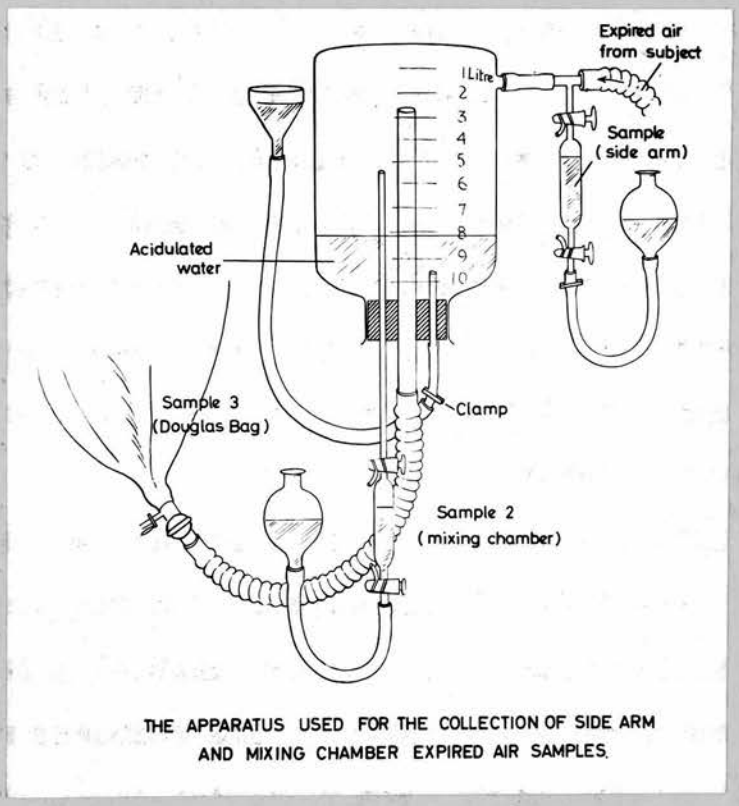

fig. 1. The apparatus used for the collection of side-arm and mixing chamber expired air samples.

1.2. Methods

The mixing chamber was constructed from a winchester bottle. The volume of the chamber could be changed to any desired capacity by raising or lowering the level of acidulated water in the bottle as shown in fig. 1.

A subject was connected to the apparatus via a two-way valve and respiratory tubing and expired air was collected during the second minute at each of two levels of exercise (6.44 km./hr. on the level and up a gradient of 15%) during twenty separate experimental sessions. Eleven experiments were performed with the mixing chamber volume held constant at 8 litres and the remainder at 2, 4 and 6 litres respectively.

Fractional (1 minute) samples were withdrawn at constant rate from the side-arm of the respiratory tubing and the mixing chamber by mercury siphoning into glass tonometers of 50 cc. capacity. The complete minute's expirate was collected into a Douglas bag. This was later emptied through a low resistance meter (Parkinson Cowan Ltd.) and a representative sample of expired air was taken in the normal way.

All the Douglas bags used in this study were of 100 L. capacity and of standard (fabric-coated vulcanised rubber) pattern (manufactured by Siebe Gorman Ltd., England). They were always examined for structural faults and tested for gross leakage before use.

Samples of expired air were analysed by the Haldane method. Duplicates were required to agree within 0.05 vols.%.

TABLE XIII.

Comparison of the rapid sampling of expired air from 1) an 8-Litre mixing chamber and 2) side-arm of the respiratory tubing prior to the mixing chamber with standard Douglas bag method.

	Mixing Chamber				Douglas Bag				Side-arm			
$\dot{V}$	O_2	CO_2	RQ	$\dot{V}O_2$	O_2	CO_2	RQ	$\dot{V}O_2$	O_2	CO_2	RQ	$\dot{V}O_2$
L./min	%	%		cc/min	%	%		cc/min	%	%		cc/min
46.6	14.40	5.52	0.90	2499	14.95	5.51	0.91	2475	14.24	6.21	0.90	2808
44.3	14.70	5.20	0.79	2541	14.71	5.32	0.82	2536	14.11	5.81	0.81	2771
46.1	14.72	5.16	0.79	2644	14.75	5.25	0.81	2619	14.21	5.74	0.82	2843
49.0	15.38	5.23	0.92	2449	15.38	5.24	0.92	2445	14.67	5.95	0.93	2752
43.1	14.37	5.46	0.79	2611	14.46	5.44	0.80	2569	13.58	6.16	0.80	2923
45.5	14.47	5.30	0.78	2719	14.56	5.30	0.79	2671	13.84	6.16	0.80	2923
47.0	14.63	5.31	0.80	2721	14.75	5.33	0.83	2659	14.26	5.78	0.84	2825
47.9	14.62	5.24	0.79	2782	14.69	5.20	0.79	2757	14.12	5.80	0.93	2993
	14.72	5.30	0.82	2621	14.78	5.32	0.83	2590	14.13	5.92	0.85	2861

TABLE XIV.

Comparison of rapid sampling of expired air from a 6, 4 and 2-Litre mixing chamber with the standard Douglas bag method.

A. 6 Litres.

		Mixing Chamber				Douglas Bag			
	$\dot{V}$	O_2	CO_2	RQ	$\dot{V}O_2$	O_2	CO_2	RQ	$\dot{V}O_2$
	L./min.	%	%		cc./min.	%	%		cc./min.
	42.9	13.97	6.54	0.92	2652	14.12	6.26	0.90	2610
	46.0	14.27	5.88	0.85	2760	14.34	5.90	0.86	2720
	24.0	15.84	4.57	0.88	1080	15.75	4.53	0.84	1127
Average		14.69	5.66	0.88	2164	14.74	5.56	0.87	2152

% error = 0.5

B. 4 Litres.

	42.5	14.31	5.86	0.85	1549	14.36	5.91	0.87	2523
	47.0	14.61	5.69	0.87	2683	14.61	5.76	0.88	2675
	20.6	15.00	4.74	0.75	1274	15.05	4.66	0.74	1264
Average		14.61	5.43	0.82	2169	14.67	5.44	0.83	2154

% error = 0.7

C. 2 Litres

	42.8	14.14	5.92	0.84	2641	14.35	5.78	0.84	2556
	23.2	15.00	4.74	0.75	1274	15.05	4.66	0.74	1264
	19.3	14.81	4.87	0.75	1090	15.42	4.24	0.72	989
	23.2	15.03	4.95	0.80	1253	15.59	4.53	0.81	1133
Average		14.75	5.12	0.79	1565	15.10	4.80	0.77	1486

% error = 5.3

TABLE XV.

Comparison of rapid side-arm sampling of expired air with the standard Douglas bag method at low ventilation rates.

		Douglas Bag				Side-arm			
	$\dot{V}$ L/min	$\%O_2$	CO_2 %	RQ	$\dot{V}O_2$ cc/min.	O_2 %	CO_2 %	RQ	$\dot{V}O_2$ cc/min.
	19.9	15.16	4.56	0.74	1065	15.29	4.46	0.74	1046
	23.2	15.05	4.66	0.74	1264	14.69	4.97	0.75	1345
	23.2	15.59	4.53	0.81	1133	14.86	4.74	0.73	1308
Aver-age		15.27	4.58	0.76	1154	14.95	4.72	0.74	1233

% error = 6.4

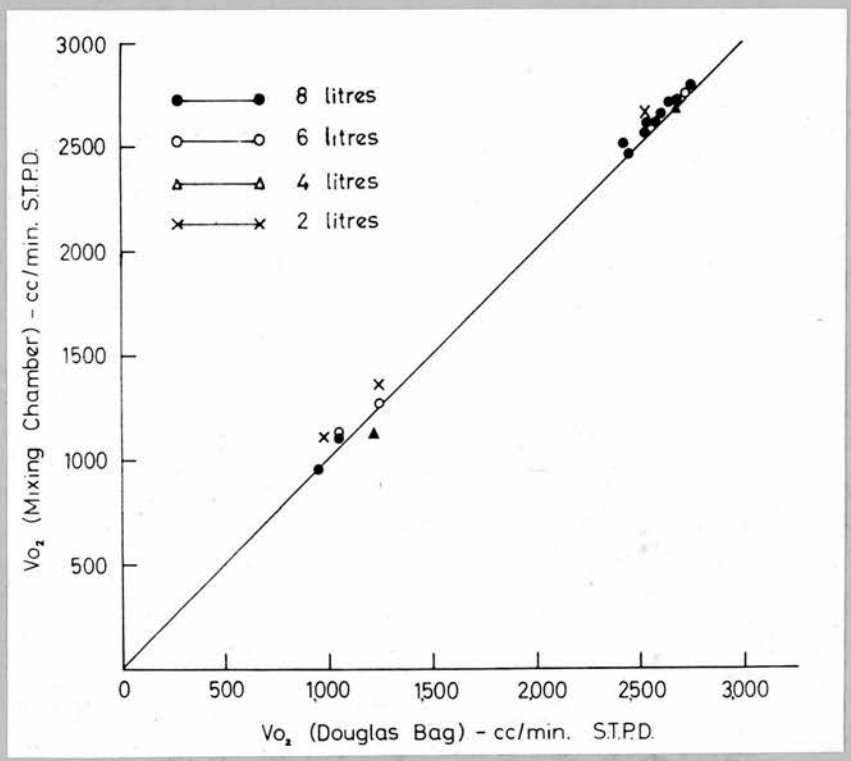

fig. 2. A comparison of the O_2-uptake values obtained from measurements of expired air using the mixing chamber and Douglas bag techniques.

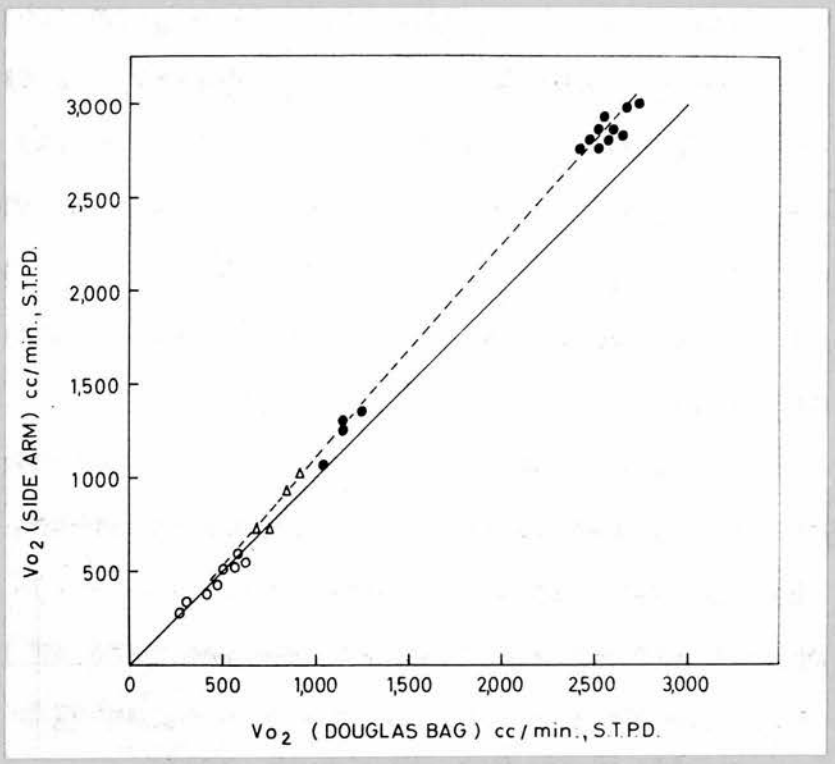

fig. 3. A comparison of O_2-uptake values obtained from measurements of expired air using the side-arm sampling and Douglas bag technique.

o o Donald et al. (1954)

△ △ " "

● ● Davies (1965)

1.3. Results

The results are summarised in tables XIII, XIV and XV.

1.4. Discussion

It is clear from the results that fractional one-minute samples of expired air can be withdrawn from a mixing chamber at both high and low ventilation rates, provided its volume does not fall below four litres. During the changing state of early exercise it introduced a small (< 1%) but insignificant error into the calculation of O_2 uptake when compared to the standard Douglas bag method (fig. 2), the standard difference between a pair of measurements being 31 mls. (table XIII).

In contrast, the side-arm sampling technique of Donald et al. (1954) introduced a considerable error. At high and low ventilation rates the mean error was 10.5% and 6.4% with a standard difference between the two sets of readings of 271 mls. and 79 mls. respectively (tables XIII and XV). At the lower O_2 uptake the error is less systematic, but as the intensity of exercise is increased, a definite pattern begins to emerge (fig. 3), the exchange ratio remains constant, but the side-arm method gives a consistently higher O_2 uptake value than the Douglas bag method. This would suggest that the side-arm device begins to collect something approaching an alveolar rather than a true representative sample of mixed expired air. This is perhaps not difficult to understand if one examines the method in detail: During inspiration the latter part of the previous expiration will fill the respira-

tory tubing leading to the mixing chamber and this will not be removed until the onset of the next expiration, but the mercury in the tonometer tube will be falling at a constant rate quite independently of these respiratory changes. Thus, for the whole of the inspiratory and latter part of the expiratory phase of respiration the side-arm will be acting as an end tidal air sampling device. The large systematic error produced by this means will tend to mask the non-systematic errors likely to be produced by simultaneous changes in ventilation and oxygen extraction encountered during the changing state. At low ventilation rates it is possible, though unlikely, that the proportion of alveolar to dead space air closely reflects the composition of expired air, but as flow rate increases during exercise of high intensity, this will certainly not be true. The rates of time spent by alveolar and dead space air in the respiratory tubing will increase disproportionately and this will be reflected in the composition of air withdrawn by any constant sampling device placed in the portion of the respiratory tubing near the subject.

Clearly, for accurate measurement of minute-to-minute changes during exercise, especially of high intensity, the side-arm sampling method has little to recommend it. If fractional collection is required during the changing state of exercise, then the method of Bock and his co-workers in conjunction with a Tissot for continuous monitoring of ventilation can safely be used, provided the volume of the chamber is greater than four litres. Below this volume level

2. Storage of expired air

2.1. Introduction

During laboratory and field investigation work, it is often not practicable to analyse samples of expired air immediately and not possible to transfer them directly into glass tonometer tubes. A well-known source of error on such occasions is the rapid loss of CO_2 due to diffusion, especially when rubber bladders (Rahaman and Durnin, 1964) and Douglas bags (Shepherd, 1955) are used. Consolazio et al. (1963) claim that this source of inaccuracy can be reduced by the use of oiled syringes, but few systematic studies have been carried out comparing directly the performance of different storage containers under the same standardised laboratory conditions. In this study, both long-term effects of gas storage in tonometers, collected over mercury and acidulated water (Garry et al., 1952) and the short-term performance of butyl rubber bladders, Douglas bags and syringes have been investigated and compared directly.

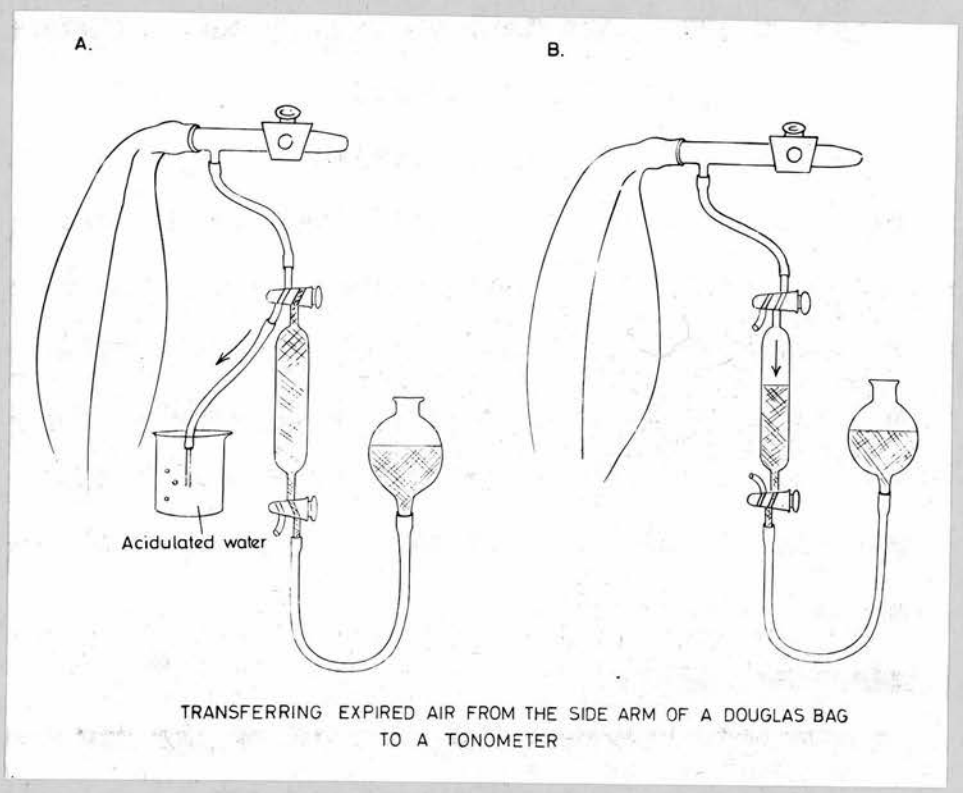

fig. 4. Apparatus used for transferring expired air from the side arm of a Douglas bag to tonometer tube. This method ensured that the gas was expelled immediately following the release of the Hoffman clamp on the side arm and the application of pressure on the bag and risk of contamination was avoided.

2.2. Methods

Short-term storage:

A standard gas mixture was delivered from a 500-litre Douglas bag and collected into the following containers:

(1) 12 oiled syringes.

(2) 3 100-litre Douglas rubber bags (Siebe-Gorman Ltd., standard pattern).

(3) 3 butyl rubber bladders.

All containers were randomly selected from those which had been in routine use in this laboratory for the past two years and were examined carefully for structural faults and leaks in the manner previously described (page 4). Samples were withdrawn from the containers into tonometer tubes and analysed for O_2 and CO_2 content at the times listed in table XVI by the Haldane method.

Long-term storage:

A similar procedure was adopted to the one described above. Gas samples were collected from the side-arm of a 100-litre Douglas bag containing expired air by either displacement of mercury or acidulated water into each of ten tonometer tubes by the method shown in fig. 4 and analysed at various time intervals as shown in table XVII.

2.3. Results

The results are summarised in tables XVI and XVII.

TABLE XVI.

Short-term storage and diffusion of carbon dioxide.

Time (hours)	Rubber (KM) Bladders (n = 3)		Douglas Bags (n = 3)		Syringes (n = 12)	
	$\%O_2$	$\%CO_2$	$\%O_2$	$\%CO_2$	$\%O_2$	$\%CO_2$
0	14.21	4.54	14.23	4.54	14.21	4.55
½	14.27	4.48				
1	14.27	4.45	14.26	4.54	14.22	4.52
2	14.32	4.32	14.23	4.52	14.19	4.55
4	14.40	4.11				
5			14.29	4.44	14.20	4.53
8	14.54	3.67	14.32	4.39	14.23	4.50
24	15.08	2.23	14.44	4.07	14.36	4.38
30					14.31	4.33

n = number of experiments for each storage container.

TABLE XVII.

Long-term storage and diffusion of carbon dioxide.

Time	Glass Tonometers			
(Days)	(Mercury)		(Acidulated water)	
	$\%O_2$	$\%CO_2$	$\%O_2$	$\%CO_2$
0	13.97	4.85	13.97	4.83
3	13.98	4.91	13.97	4.86
7	13.99	4.89	13.97	4.85
14	13.95	4.92	13.96	4.89
28	13.95	4.91	13.93	4.85
56	13.95	4.90	13.97	4.79

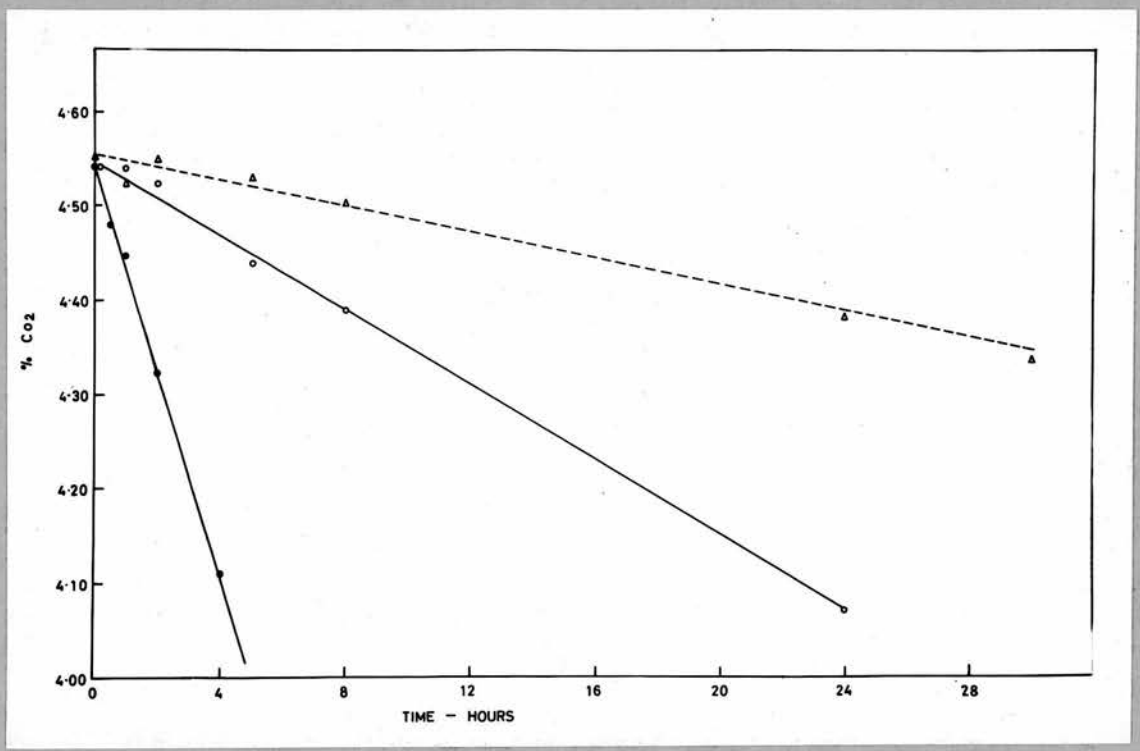

fig. 5. The selective loss of CO_2 from expired air samples stored in rubber bladders ●——●, Douglas bags o——o, and syringes △——△.

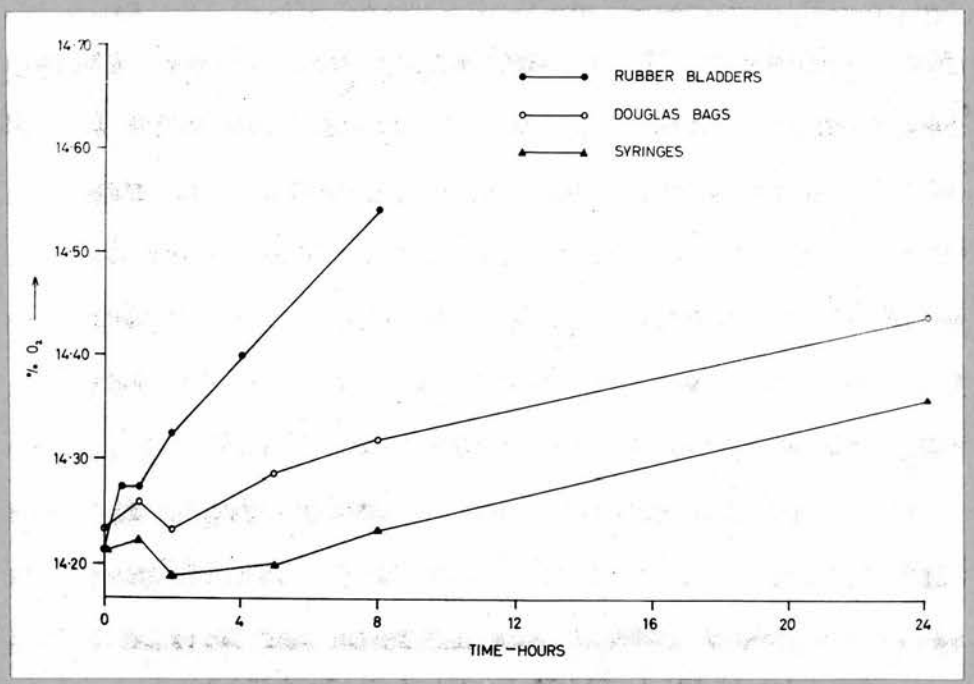

fig. 6. The selective loss of O_2 from expired air samples stored in the above containers.

2.4. Discussion

The selective loss of CO_2 from butyl rubber bladders is approximately 0.11%/hr. and for Douglas bags 0.02%/hr. (fig. 5). At thirty minutes there was a considerable change in CO_2 concentration within the rubber bladder. Thus, originally the CO_2 concentration was 4.54% changed to 4.48% within half-an-hour. At the fourth hour it was 4.11% and finally became 2.23% after twenty-four hours' storage. The corresponding changes in O_2 concentration were 14.21%, 14.27%, 14.40% and 15.08% respectively. The Douglas bags, on the other hand, showed no significant loss of CO_2 concentration after two hours (4.54% to 4.52%), but after twenty-four hours the CO_2% had fallen to 4.07%. In the same time period the O_2 concentration had risen from 14.23% to 14.44% (fig. 6).

The possible factors which govern these different rates of diffusion of O_2 and CO_2 have been investigated and summarised by Shepherd (1955) and Rahaman and Durnin (1964). The main cause of the difference between O_2 and CO_2 is the higher solubility of CO_2 in rubber. Shepherd (1955) has shown that the ratio of solubilities of CO_2, O_2, and N_2 is approximately 10 : 2 : 1 and suggests that the gases become dissolved at the proximal surfaces and evaporate at the distal surface after diffusing through the intervening rubber. In practice this can be minimised by filling the bladders or Douglas bags prior to use with expired air and not allowing them to become over-inflated during the actual period of metabolic measurement. Rahaman and Durnin (1964) suggest a further precaution to reduce the loss of CO_2 from rubber bladders

if immediate analysis is not possible. The method consists of storing the bladder within a polythene bag filled with expired air. From their published figures the differences produced by this means would appear to be only marginal during the first thirty minutes and if longer time intervals are involved, it necessitates a correction factor being used. Obviously, on theoretical grounds, it is much better to store the bladders in environments closely resembling their own concentration of gas mixture than allowing them to be exposed to the atmospheric air, but in practice the method still entails the use of a correction factor and it is laborious and time-consuming. There is no question that in the laboratory rubber bladders must be analysed or transferred to glass tonometers immediately. In the field, though samples cannot be analysed they can be transferred either to tubes by displacement of acidulated water (see Garry et al., 1955, fig. 10, p54) or oiled syringes, with the minimum of difficulty. These methods are preferable to any other form of storage treatment in the field situation. Only if for some unforeseen reason the sample has to remain inside the bladder should a correction be made (cf. table XVI and fig. 5) and this should be applied with care and a certain amount of reservation.

The oiled syringes show no significant loss of CO_2 or O_2 during the first eight hours of storage. This confirms the finding of Consolazio et al. (1963). At thirty hours the O_2 concentration had risen by 0.1% and the CO_2 had fallen by 0.22%. For laboratory and field investigation, they make

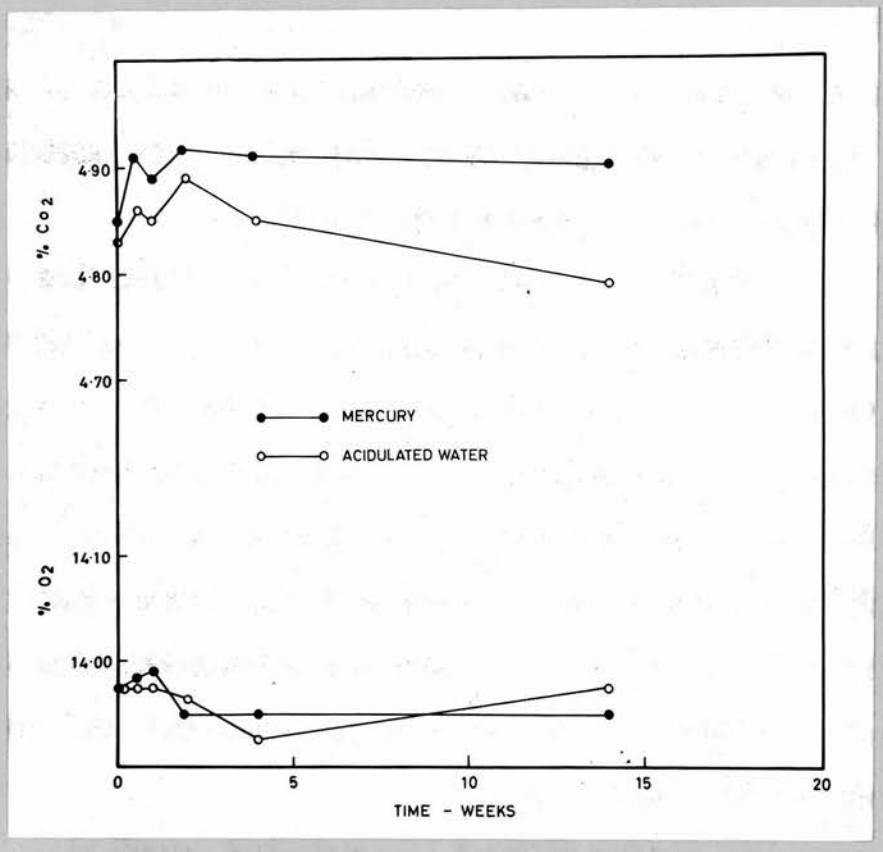

fig. 7. The selective loss of O_2 and CO_2 from expired samples stored in glass tonometer over mercury and acidulated water.

an excellent storage container, especially where the rate of energy expenditure is determined solely by using the O_2 content of the expired air (Weir, 1949). Syringes can be used in conjunction with Douglas bags or rubber bladders or mixing chamber methods of collecting expired air. They are simple to use, but some care should be taken to flush out the syringe thoroughly with samples of the expired air prior to collecting the sample for analysis.

Undoubtedly, of all the storage containers tested, the glass tonometers were superior in their ability to retain mixtures of CO_2, O_2 and N_2. Even after fifty-six days of storage both the acidulated water and mercury samples were still relatively unchanged (fig. 7). In field and laboratory situations where very accurate determination of respiratory quotients and oxygen uptakes are required, then every effort should be made either to analyse or store the gas samples in glass tubes immediately.

3. Analysis of expired air

3.1. Introduction

The Haldane gas analyser has been accepted for nearly fifty years as the standard chemical means for the analysis of the O_2 and CO_2 content of expired air. However, with the advent of the paramagnetic O_2 analyser of Pauling et al. (1946) becoming commercially available, several laboratories have begun to change to this more automatic and rapid (physical) method of gas analysis.

The instrument is simple to use and does avoid the laborious and time-consuming analysis technique of the standard Haldane Method. It is also claimed to be as reliable, but surprisingly few attempts have been made to evaluate the accuracy of the analyser. Of the literature available, only Consolazio et al. (1963) using a small number of samples have compared its performance with that of an established chemical method.

In this study an attempt has been made to repeat and extend their work. Two hundred samples of expired air obtained from an exercising subject have been analysed using both the paramagnetic O_2 meter (Beckman Instruments Ltd.) and the standard (Lloyd) Haldane apparatus and the results have been compared directly.

TABLE XVIII.

Comparison between duplicate Beckman analysis and the Haldane method. A portion of the data showing the daily distribution of results.

HALDANE			BECKMAN	DIFFERENCE
	$\%O_2$	$\%CO_2$	$\%O_2$	
1.	16.84	3.80	16.61	-0.23
2.			16.51	-0.33
1.	14.97	4.84	14.74	-0.23
2.			14.92	-0.05
1.	13.96	5.39	13.85	-0.11
2.			13.85	-0.11
1.	14.15	5.74	14.07	-0.08
2.			14.07	-0.08
1.	14.12	5.97	14.05	-0.07
2.			14.14	+0.02
1.	14.16	6.15	14.02	-0.14
2.			14.09	-0.07
1.	14.36	6.16	14.52	+0.16
2.			14.45	+0.09
1.	16.60	5.29	16.54	-0.06
2.			16.52	-0.08
1.	17.12	3.95	17.22	+0.10
2.			-	-
1.	17.04	3.91	17.05	+0.01
2.			17.02	-0.02

TABLE XIX.

The accuracy of the Beckman E_2 analyser using high and low concentrations of O_2.

A - Separately			B - In rotation		
Gas Concentration	Syringe No.	$\%O_2$	Order	Syringe No.	$\%O_2$
Low	162	9.62	Air		20.92
	155	9.65	1	162	9.62
	125	9.71	2	137	14.12
	127	9.68	3	139	17.85
	151	9.66	4	155	9.65
Haldane	-	9.64	5	131	14.12
Medium	137	14.12	6	392	17.82
	131	14.12	7	157	14.15
	157	14.15	8	125	9.71
	132	14.12	9	153	17.84
	135	14.17	10	127	9.68
Haldane	-	14.16	11	132	14.12
High	139	17.85	12	151	9.66
	392	17.82	13	154	17.82
	153	17.84	14	135	14.17
	154	17.82	15	126	17.83
	126	17.83	Air		20.94
Haldane	-	17.91			

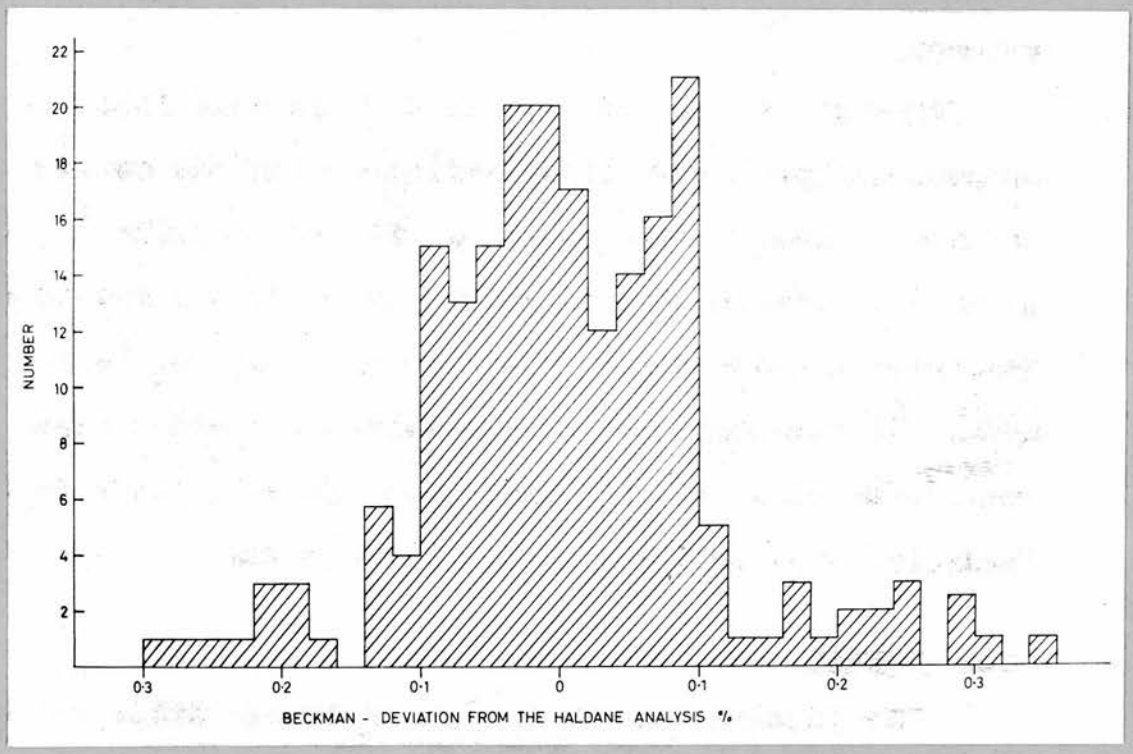

fig. 9. Histogram showing the deviation of the Beckman O_2 analysis from the standard Haldane method.

3.2. Methods

Duplicate expired air samples were collected from an exercising subject over a period of four weeks using the standard Douglas bag method. The samples were analysed immediately for O_2 content by the Lloyd-Haldane and Beckman methods.

Expired air gas samples were introduced into the Beckman analyser from oiled syringes with the chamber of the meter under partial vacuum. The calibration of the meter was effected in the normal way: N_2 was passed through the inner chamber to fix the zero and 99.6% O_2 to fix the span. The calibration was periodically checked using compressed air. All readings were taken in the steady state condition when actual gas flow had ceased.

3.3. Results

The results are summarised in tables XVIII and XIX and fig. 8.

3.4. Discussion

The reasons for occasional large discrepancies (± 0.35 vols.%) between the two methods shown in fig. 8. are difficult to analyse. They could have arisen from the fact that though the Beckman analysis was performed by the same person each day, the Haldane analyses were shared between three different people, but even reversing the procedure, or using different combinations of Haldane operations, or insisting that duplicates were done on other machines by a different person, or even allowing one person to be responsible for the complete analysis (table XVIII) did not change the daily distribution of the results which was always similar to that shown for the whole investigation in fig. 8. The Beckman often gave slightly high or low, but never inconsistent results, when tested with gas mixtures of known concentrations (table XIX). It would therefore seem unlikely that sudden large errors in gas analysis could arise from the instability or unreliability of the analyser during the actual analysis periods. One is inclined to the view, therefore, that these occasional errors must be due to a (human) error in the collection of the gas or storage, or in actually introducing the gas sample into the Haldane apparatus prior to analysis.

Thus, from the results, it might be difficult to claim that the Beckman E_2 O_2 analyser is as accurate as the conventional Haldane method. Nevertheless, they do show that it does provide a simple, rapid and reliable means of analysing the O_2 content of expired air. Of the 200 expired

air samples analysed on the instrument 80% fell within 0.15 vols. % of the figure obtained on the Lloyd-Haldane apparatus. This would involve a small ($\pm$ 2%) and insignificant error when estimating energy expenditure using the Weir formula. For most purposes this will be sufficient and thus the use of oiled syringes in combination with the paramagnetic O_2 analyser provide a useful and powerful tool in the field of metabolic physiology. However, in cases where a greater accuracy $\pm$ 0.15 Vols. % O_2 content is required, expired air should be analysed by the conventional chemical technique.

Summary and Conclusions

1. Fractional collection can be performed by inserting a mixing chamber of four litres or more into the respiratory gas sampling system. Side-arm sampling from the respiratory tubing leading to the mixing chamber introduces an error of 10.5% at high and 5.3% at low ventilations, into the estimation of energy expenditure. The error was found to be systematic and probably resulted from the greater volume of alveolar air being sampled by this technique compared with the standard Douglas bag method.

2. The selective ~~to~~ loss of CO_2 from butyl rubber bladders, Douglas bags and syringes was found to be 0.11%/hr., 0.2%/hr. and 0.007%/hr., respectively during an eight-hour period. Loss of CO_2 during the first thirty minutes was high in the case of the bladders and they were found to be very unsatisfactory storage containers. Douglas bags showed a negligible loss of CO_2 during the first two hours, but the concentration began to fall shortly thereafter. Syringes, on the other hand, showed no appreciable decline of CO_2 until after the eighth hour of storage. Samples collected in glass tonometers by mercury siphoning and displacement of acidulated water still maintained their concentrations of O_2 and CO_2 after fifty-six days of storage.

3. The Pauling (Beckman E_2) analyser was found to be an accurate, simple and fast method of estimating the O_2 concentration in expired air. The accuracy of the analyser was found to be $\pm$ 0.15 vol.% when compared with the conventional Haldane gas analysis method.

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Appendix 2

THE HEART RATE DURING TRANSITION FROM REST TO EXERCISE IN RELATION TO EXERCISE TOLERANCE

TABLES OF RESULTS

TABLE XX.

Basic data.

(referred to in Part II)

Subject	Speed km./hr.	Gradient (tan Angle %)	$\dot{V}_E$	$\dot{V}O_2{}^{65}$ cc. STPD	f breaths	EHR beats/min.
R.M.M.	Rest		6.40	267	17	68
Wt=63.85	6.44	0	21.58	1149	22	110
		1	22.65	1265	24	112
		3	27.57	1576	27	122
		5	30.50	1095	26	132
		7	33.96	1840	29	145
		9	40.29	2104	31	151
		12	51.32	2555	35	174
		15	65.18	2800	38	187
J.T.H.	Rest		7.99	258	14	76
Wt=89.87	6.44	1	29.45	1350	20	123
		3	31.62	1377	21	124
		5	36.26	1613	23	129
		7	40.18	1776	23	141
		9	42.00	1944	22	151
		12	53.71	2377	29	175
		15	67.36	2850	35	192
D.S.O.	Rest		6.46	282	9	68
Wt=71.09	6.44	1	23.19	1243	19	104
		3	25.67	1475	19	106
		5	29.16	1673	20	114
		7	32.50	1864	23	119
		9	36.54	2050	25	128
		12	42.02	2390	28	146
		15	47.74	2703	22	154
F.E.G.	Rest		6.53	327	-	53
Wt=62.99	6.44	1	22.12	1296	15	88
		3	25.97	1426	17	93
		5	28.92	1680	17	97
		7	32.00	1893	18	104
		9	36.97	2160	19	117
		12	44.71	2644	22	131
		15	49.61	3036	22	144
W.J.S.	Rest		8.76	278	9	62
Wt=75.40	6.44	1	21.68	1166	12	107
		3	25.18	1328	13	112
		5	29.53	1579	13	121
		7	33.06	1769	15	132
		9	35.14	1960	14	150
		12	49.68	2490	22	171
		15	61.36	2875	31	186

Table XX - basic data (contd.)

Subject	Speed km./ hr.	Grad-ient (tan Angle %)	$\dot{V}_E$ Litres	$\dot{V}O_2{}^{65}$ cc. STPD	f breaths /min.	EHR beats/ min.
R.W.L.	Rest	0	4.36	247	9	81
Wt=61.10	4.83	0	12.63	987	10	109
	6.44	1	15.32	1101	11	136
		3	19.41	1437	14	146
		5	23.01	1692	15	159
		7	28.92	2012	19	178
		9	31.46	2179	18	183
		12	43.54	2507	24	196
I.R.F.	Rest		7.90	286	9	86
Wt=83.3	6.44	0	22.82	1135	15	116
		1	28.63	1253	20	129
		3	31.67	1438	21	130
		5	33.33	1579	20	138
		7	40.49	1874	22	156
		9	54.88	2252	33	177
		12	68.14	2621	45	187
C.F.J.R.	Rest		6.31	261	14	68
Wt=77.37	6.44	1	21.71	1140	17	95
		3	25.21	1337	19	109
		5	30.26	1531	20	104
		7	33.67	1740	23	113
		9	39.52	2022	25	132
		12	47.66	2410	27	152
		15	59.95	2780	31	164
A.F.M.	Rest		6.21	284	11	54
Wt=6625	6.44	1	18.85	1274	12	89
		3	22.40	1437	13	101
		5	24.28	1557	13	107
		7	30.75	1937	16	115
		9	34.69	2174	18	123
		12	38.24	2405	19	125
		15	45.42	2821	20	139
A.E.C.C.	Rest		6.24	196	11	61
Wt=67.95	6.44	1	24.00	1203	20	110
		3	29.19	1483	20	128
		5	32.14	1601	21	142
		7	40.72	1929	21	159
		9	46.90	2216	21	171
		12	60.68	2658	22	183

TABLE XXI.

Basic data

Subject: C.T.M.D. Age: 30 yrs. Wt: 70.02 kg. Ht: 175.00 cm.

Experiment No.	Speed km./hr.	Gradient %	Time mins.	$\dot{V}_E$ Litres	OE %	CO_2D %	$\dot{V}O_2^{65}$ cc. STPD	f breaths/min	EHR beats/min.
Expt.1	6.44	0	Rest	3.48	6.45	4.83	205	8	65
			0.5	12.08	6.77	4.89	759	-	103
			1.5	14.08	7.84	5.15	1025	-	108
			2.5	15.35	7.83	5.52	1115	-	111
			3.5	16.74	7.81	5.79	1213	-	111
			5.0	15.04	7.74	5.94	1101	11	114
			6.5	12.53	6.43	5.37	748	-	-
			8.5	6.18	4.63	4.47	268	-	-
			15.5	4.92	4.90	4.27	224	-	-
Extp.2	"	"	Rest	-	-	-	-	-	-
			0.13	9.80	5.58	4.16	508	-	104
			0.75	12.34	7.83	5.03	896	-	96
			1.75	15.05	8.09	5.38	1130	-	100
			2.75	15.28	8.35	5.65	1184	-	103
			3.75	15.94	7.60	5.59	1124	-	102
			5.13	17.95	7.23	5.47	1205	15	103
			6.5	10.68	6.58	4.41	652	-	-
			7.5	9.56	4.85	5.42	431	-	-
			14.5	5.01	5.07	4.45	236	-	-
Expt.3	"	"	Rest	4.03	5.66	4.43	212	8	63
			0.25	13.22	5.85	4.23	718	-	108
			1.0	12.77	7.37	4.77	873	-	96
			2.0	15.18	7.68	5.22	1082	-	100
			3.0	16.16	7.52	5.36	1127	-	103
			4.0	16.84	7.41	5.51	1158	-	106
			5.25	17.64	6.88	5.43	1126	12	103
			7.0	8.86	5.73	5.21	514	-	-
			8.5	5.17	4.50	4.32	236	-	-
			15.0	4.65	5.06	4.43	236	-	-
Expt.4	"	"	Rest	4.15	5.80	4.43	224	7	57
			0.38	12.00	5.84	4.49	650	-	93
			1.25	16.27	7.55	4.97	1140	-	98
			2.25	16.09	7.52	5.25	1123	-	103
			3.25	16.98	7.38	5.31	1163	-	101
			4.25	16.78	7.30	5.50	1137	-	102
			5.38	17.60	7.38	5.47	1148	12	103
			7.5	8.61	5.52	4.75	441	-	-
			9.5	5.68	4.45	4.10	256	-	-
			15.5	4.93	4.73	4.17	216	-	-

Table XXI - basic data (contd.)

Experiment No.	Speed km/hr.	Gradient %	Time mins.	$\dot{V}_E$ Litres	OE %	CO_2D %	$\dot{V}O_2$ 65 cc. STPD	f breaths	EHR beats/min.
Expt.5	6.44	3	Rest	4.69	5.46	3.89	238	8	68
			0.5	14.30	6.70	4.79	888	-	106
			1.5	16.68	8.02	5.42	1242	-	114
			2.5	20.16	7.93	5.79	1483	-	117
			3.5	21.12	7.10	5.73	1392	-	121
			5.0	21.26	7.07	5.70	1395	14	123
			6.5	14.23	6.38	5.75	1843	-	-
			14.0	6.11	4.74	4.28	268	-	-
Expt.6	"	"	Rest	5.37	4.71	4.00	234	10	69
			0.13	9.56	4.76	3.78	424	-	104
			0.75	16.23	6.82	4.98	1027	-	103
			1.75	19.85	7.35	5.14	1354	-	114
			2.75	20.73	7.29	5.48	1402	-	116
			3.75	19.58	7.04	5.60	1379	-	118
			5.13	21.61	7.10	5.75	1424	14	119
			6.5	14.18	5.40	5.20	776	-	-
			7.5	9.39	4.38	4.38	415	-	-
			14.5	6.68	4.43	3.85	275	-	-
Expt.7	"	"	Rest	4.43	5.75	4.45	236	8	73
			0.25	13.74	6.09	4.22	776	-	104
			1.0	16.17	7.76	5.09	1164	-	117
			2.0	19.32	7.63	5.72	1368	-	119
			3.0	20.90	6.68	5.57	1295	-	121
			4.0	21.25	7.08	5.57	1397	-	124
			5.25	20.72	6.90	5.68	1316	13	125
			7.0	10.36	5.68	5.48	570	-	-
			15.0	5.54	4.91	4.47	252	-	-
Expt.8	"	"	Rest	4.64	5.20	4.35	224	9	70
			0.38	14.26	6.13	4.65	812	-	108
			1.25	17.93	7.40	5.45	1231	-	113
			2.25	18.79	7.58	5.87	1321	-	121
			3.25	18.86	7.85	6.10	1374	-	122
			4.25	20.49	7.57	6.13	1439	-	122
			5.38	21.28	7.12	6.17	1415	13	123
			7.5	9.72	4.89	5.11	447	-	-
			9.5	5.82	4.12	4.23	279	-	-
			15.5	5.52	4.52	4.10	231	-	-
Expt.9	6.44	6	Rest	4.28	5.82	4.54	231	8	76
			0.5	15.01	7.02	5.83	978	-	116
			1.5	20.13	7.44	5.95	1577	-	135
			2.5	24.37	7.50	6.11	1696	-	140
			3.5	24.52	7.51	6.38	1708	-	144
			5.0	25.27	7.52	6.53	1785	14	150
			6.5	19.85	5.93	5.88	1092	-	-
			14.0	6.07	4.70	4.52	264	-	-

Table XXI - basic data (contd.)

Experiment No.	Speed km/hr.	Gradient %	Time mins.	$\dot{V}_E$ Litres	OE %	CO_2D %	$\dot{V}O_2$ 65 cc. STPD	f breaths	EHR beats/min.
Expt.10	6.44	6	Rest	5.10	4.91	4.09	232	10	76
			0.13	13.76	4.87	4.11	624	-	112
			0.75	17.44	7.50	5.35	1213	-	121
			1.75	21.91	7.56	5.79	1487	-	135
			2.75	23.06	7.78	6.55	1665	-	143
			3.75	24.82	6.96	6.49	1602	-	144
			5.13	24.74	7.45	6.69	1719	13	148
			6.5	17.86	5.16	5.58	933	-	-
			7.5	8.18	4.09	4.48	339	-	-
			14.5	6.17	4.56	4.25	261	-	-
Expt.11	"	"	Rest	4.82	4.54	3.96	203	9	72
			0.25	13.20	5.43	4.42	612	-	112
			1.0	19.27	7.35	5.11	1314	-	121
			2.0	24.88	7.37	5.83	1702	-	130
			3.0	26.54	6.94	6.09	1709	-	135
			4.0	25.62	6.91	6.10	1643	-	137
			5.25	27.85	6.49	6.00	1690	14	143
			7.0	14.54	5.04	5.18	741	-	-
			8.5	8.92	3.57	3.92	363	-	-
			15.0	6.55	3.86	3.94	234	-	-
Expt.12	"	"	Rest	4.79	4.69	3.77	209	9	67
			0.38	13.55	5.99	4.81	753	-	107
			1.25	20.98	7.46	5.36	1452	-	120
			2.25	25.36	7.08	5.71	1666	-	130
			3.25	24.65	7.05	5.94	1613	-	135
			4.25	25.89	6.95	6.12	1669	-	136
			5.38	28.42	6.70	6.13	1768	14	137
			7.5	12.64	4.09	5.26	523	-	-
			9.5	6.20	3.79	3.92	257	-	-
			15.5	6.15	3.91	3.88	223	-	-
Expt.13	6.44	9	Rest	4.38	5.52	4.41	225	8	76
			0.5	17.92	7.20	5.00	1197	-	131
			1.5	26.78	6.88	5.14	1709	-	146
			2.5	31.45	6.72	5.97	1961	-	154
			3.5	31.63	6.62	6.16	1943	-	159
			5.0	31.23	6.91	6.44	2003	15	163
			7.0	19.30	5.19	5.61	929	-	-
			9.0	9.25	3.94	4.53	369	-	-
			18.0	5.91	4.78	4.36	263	-	-
Expt.14	"	"	Rest	5.33	5.03	4.07	248	10	78
			0.13	17.72	4.92	3.87	904	-	109
			0.75	22.20	6.95	5.25	1432	-	134
			1.75	31.54	6.64	5.64	1943	-	152
			2.75	30.92	6.76	5.99	1940	-	156
			3.75	31.10	6.79	6.24	1960	-	163
			5.13	31.61	6.88	6.50	2017	16	166
			8.0	13.13	4.93	5.45	601	-	-
			11.0	12.20	4.09	4.23	505	-	-
			17.0	5.27	4.79	4.18	234	-	-

Table XXI - basic data (contd.)

Experiment No.	Speed km/hr.	Gradient %	Time mins.	$\dot{V}_E$ Litres	OE %	CO_2D %	$\dot{V}O_2{}^{65}$ cc. STPD	f breaths	EHR beats/min.
Expt.15	6.44	9	Rest	4.18	5.01	4.09	208	8	76
			0.25	14.32	5.57	4.24	554	-	-
			1.0	21.30	7.45	5.16	1473	-	-
			2.0	29.48	6.89	5.58	1885	-	-
			3.0	29.74	6.69	6.09	1847	-	-
			4.0	33.61	6.48	6.00	2021	16	-
			9.0	11.29	4.56	4.89	478	-	-
			19.0	5.32	4.64	4.11	267	-	-
Expt.16	"	"	Rest	4.35	4.96	4.04	201	9	73
			0.38	13.70	6.53	4.59	831	-	115
			1.25	26.90	6.95	5.24	1735	-	138
			2.25	32.08	6.45	5.70	1920	-	152
			3.25	30.14	6.72	6.19	1879	-	157
			4.25	33.05	6.76	6.33	2073	-	162
			5.38	31.69	6.95	6.59	2041	17	164
			9.0	10.56	4.70	5.33	461	-	-
			13.0	9.13	4.16	4.19	384	-	-
			15.0	5.81	4.33	3.86	255	-	-
			21.0	53.80	4.49	3.82	224	-	-
Expt.17	6.44	15	Rest	4.18	5.59	4.48	217	8	68
			0.5	20.83	6.36	4.79	1230	-	129
			1.5	40.60	6.14	5.66	2314	-	164
			2.5	44.83	5.43	5.78	2364	-	175
			3.5	46.59	5.61	6.10	2425	-	175
			5.0	45.81	5.74	6.22	2440	22	174
			7.0	25.11	4.18	5.31	974	-	-
			10.0	13.11	3.38	4.48	411	-	-
			18.0	6.91	4.48	4.00	287	-	-
			30.0	5.09	5.09	5.01	267	-	-
Expt.18	4.83	0	0.5	9.49	6.15	4.90	542	-	102
			2.0	10.33	7.42	5.66	711		95
			4.5	11.45	7.48	5.90	794	10	94
			6-16	59.40	4.82	4.62	265	-	-
Expt.19	"	"	1.0	10.00	7.18	5.37	666	-	82
			3.0	10.18	8.00	5.97	755	-	83
			5.0	11.41	7.42	5.83	786	9	87
			6-16	61.00	4.86	4.75	275	-	-
Expt.20	"	"	1.5	9.60	7.43	5.37	662	-	81
			4.0	11.02	7.62	5.72	780	-	85
			5.5	11.58	7.67	5.85	824	10	84
			7.0	7.86	5.48	5.04	400	-	-
			8-16	40.03	5.17	4.71	240	-	-
Expt.21	3.22	0	0.5	9.81	5.59	4.58	509	-	84
			2.0	9.50	6.75	5.13	595	-	77
			4.5	8.55	7.40	5.52	587	10	79
			6-16	54.10	5.31	4.63	266	-	-

Table XXI - basic data (contd.)

Experiment No.	Speed km/hr.	Gradient %	Time mins.	$\dot{V}_E$ Litres	OE %	CO_2D %	$\dot{V}O_2{}^{65}$ cc. STPD	f breaths	EHR beats/min.
Expt.22	3.22	0	1.0	8.05	6.91	5.14	516	-	78
			3.0	9.15	7.24	5.37	614	-	76
			5.0	9.68	6.80	5.37	611	11	77
			6-16	50.4	5.44	4.84	254	-	-
Expt.23	"	"	1.5	8.58	6.71	5.10	535	-	75
			4.0	9.45	6.40	5.12	561	-	76
			5.5	10.76	6.40	5.05	639	11	75
			7.0	6.56	3.90	4.85	359	-	-
			8-16	37.23	5.07	4.27	219	-	-
Subject: A.F.M. Age: 21 yrs. Wt: 66.26 kg. Ht: 177.50 cm.									
Expt. 1	6.44	9	Rest	5.13	4.91	3.92	252	13	43
			5.0	31.05	6.42	5.03	1956	15	106
			6-19	8.34	4.99	4.23	408	-	-
			19-21	6.14	4.45	3.49	268	-	-
Expt. 2	"	12	Rest	5.36	4.66	3.72	250	10	-
			5.0	38.18	6.31	5.03	2363	17	118
			6-16	9.25	4.86	4.08	441	-	-
			16-26	6.03	4.60	3.90	272	-	-
Expt. 3	"	15	5.0	41.79	6.38	5.14	2600	19	127
			6-16	10.37	4.79	4.55	487	-	-
			16-26	6.65	4.67	4.24	304	-	-
			Rest	4.85	4.74	3.69	230	11	-
Expt. 4	"	18	4.5	48.70	6.24	5.24	2964	-	-
			5.5	47.66	6.34	5.26	2825	21	139
			6-9	17.42	5.51	5.04	941	-	-
			9-23	6.50	4.91	4.21	313	-	-
			23-36	6.31	5.28	3.97	327	-	-
Expt. 5	11.27	12	Rest	5.71	4.34	3.42	248	10	-
			4.5	86.09	5.41	5.30	4569	-	-
			5.5	79.36	5.43	5.30	4227	31	171
			6-9	31.03	4.74	5.14	1443	-	-
			9-19	8.63	4.46	4.27	377	-	-
			19-29	6.91	4.94	4.14	334	-	-
			29-36	6.28	4.77	4.16	294	-	-

TABLE XXII.

Summary of data given in table XXI.

Subject	Speed km./hr.	Gradient %	$\dot{V}_E$ Litres	OE %	CO_2D %	R	f breaths/min.	$\dot{V}O_2$ 65 Litres STPD	O_2 deficit mls.	O_2 debt mls.	EHR beats/min.	PD beats
C.T.M.D.	3.22	0	9.7	6.87	5.31	.78	11	596	175	136	77	0
Wt.=	4.83	0	11.5	7.50	5.85	.78	10	783	398	250	87	3
70.02	6.44	0	17.0	7.31	5.57	.77	12	1145	435	665	103	2
$\dot{M}axVO_2$	"	3	21.1	7.15	5.96	.81	14	1389	600	798	120	5
= 3.09	"	6	26.5	7.05	6.33	.90	14	1704	972	1080	140	28
	"	9	31.9	6.85	6.46	.94	16	1995	-	2410	161	55
	"	15	45.8	5.74	6.22	1.09	22	2465	-	3000	174	52
A.F.M.	"	9	31.1	6.42	5.03	.79	15	1956	-	1837	104	2
Wt.=	"	12	38.2	6.31	5.03	.80	17	2363	-	1783	116	3
66.26	"	15	41.8	6.38	5.14	.81	19	2600	-	2574	126	7
$\dot{M}axVO_2$	"	18	48.2	6.29	5.25	.85	21	2972	-	3449	135	6
= 5.43	11.27	12	82.7	5.42	5.30	.98	31	4227	-	6497	168	60